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Access DB# _____

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: Khatol Shahnan-Shah Examiner #: 78526 Date: 5/6/03
Art Unit: 1645 Phone Number 30 8-8896 Serial Number: 09/975,020
Mail Box and Bldg/Room Location: 8D-16 Results Format Preferred (circle): PAPER DISK E-MAIL
8E-12

If more than one search is submitted, please prioritize searches in order of need.

****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: See attached Rib Shunt

Inventors (please provide full names): _____

Earliest Priority Filing Date: 10/12/2001

***For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.**

Please search claim 1-28 See attached. Including authors and meeting key words highlighted

Thanks.

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PTO-1590 (8-01)

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BIBDATASHEET

Bib Data Sheet

CONFIRMATION NO. 7596

SERIAL NUMBER	FILING DATE	CLASS	GROUP ART UNIT	ATTORNEY DOCKET NO.
09/975,020	10/12/2001 RULE	424	1645	P66822US0 (WRAIR 98-40/46

APPLICANTS

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Kenneth H. Eckels, College Park, MD;
William R. Ballou, Silver Spring, MD;

** CONTINUING DATA **********

** FOREIGN APPLICATIONS **********

IF REQUIRED, FOREIGN FILING LICENSE GRANTED
** 11/13/2001

Foreign Priority claimed ☐ yes ☐ no 35 USC 119 (a-d) conditions met ☐ yes ☐ no ☐ Met after Allowance Verified and Acknowledged _____ Examiner's Signature _____ Initials	STATE OR COUNTRY	SHEETS DRAWING	TOTAL CLAIMS	INDEPENDENT CLAIMS
	MD	1	28	2

ADDRESS
Office of the Staff Judge Advocate
U.S. Army Medical Research and Materiel Command
ATTN: MCMR-JA (Ms. Elizabeth Arwine)
504 Scott Street
Fort Detrick , MD
21702-5012

TITLE
Microfluidized leishmania lysate and methods of making and using thereof

FILING FEE RECEIVED	FEES: Authority has been given in Paper No. _____ to charge/credit DEPOSIT ACCOUNT No. _____ for following:	☐ All Fees ☐ 1.16 Fees (Filing) ☐ 1.17 Fees (Processing Ext. of time) ☐ 1.18 Fees (Issue)

We Claim:

1. A method of preparing a microfluidized lysate preparation comprising microfluidizing a slurry of at least one *Leishmania* parasite through a chamber and disrupting the leishmania parasite with a sudden release of pressure.

2. The method of claim 1, further comprising heat treating the microfluidized lysate preparation.

3. The method of claim 1, wherein the *Leishmania* parasite is *L. tropica, L. mexicana, L. guyanensis, L. braziliensis, L. major, L. donovani, L. chagasi, L. amazonensis, L. peruviana, L. panamensis, L. pifanoi, L. infantum,* or *L. aethiopica.*

4. A microfluidized lysate preparation made by the method of claim 1.

5. A skin test antigen assay for detecting whether a subject had been exposed to a *Leishmania* parasite or was afflicted with Leishmaniasis comprising administering to the subject an antigenic amount of at least one microfluidized lysate preparation according to claim 4 and observing any immunogenic response to the microfluidized lysate preparation.

6. The skin test antigen assay of claim 5, wherein the *Leishmania* parasite is *L. tropica, L. mexicana, L. guyanensis, L. braziliensis, L. major, L. donovani, L. chagasi, L. amazonensis, L. peruviana, L. panamensis, L. pifanoi, L. infantum,* or *L. aethiopica.*

7. The skin test antigen assay of claim 5, wherein an immunogenic response indicates that the subject had been exposed to a *Leishmania* parasite or was afflicted with Leishmaniasis.

8. The skin test antigen assay of claim 5, wherein an induration of about 5 mm or greater observed indicates that the subject had been exposed to a *Leishmania* parasite or was afflicted with Leishmaniasis.

9. The skin test antigen assay of claim 5, wherein the antigenic amount of the microfluidized lysate preparation comprises about 5 μg to about 30 μg of total protein.

10. The skin test antigen assay of claim 5, wherein the antigenic amount of the microfluidized lysate preparation is administered intradermally to the volar surface of the forearm of the subject.

11. A kit comprising the microfluidized lysate preparation of claim 4 and directions for determining whether a subject has been exposed to a *Leishmania* parasite or was afflicted with Leishmaniasis.

12. The kit of claim 11, wherein the *Leishmania* parasite is *L. tropica, L. mexicana, L. guyanensis, L. braziliensis, L. major, L. donovani, L. chagasi, L. amazonensis, L. peruviana, L. panamensis, L. pifanoi, L. infantum,* or *L. aethiopica*.

13. The kit of claim 11, further comprising at least one pharmaceutical for treating systemic anaphylaxis.

14. The kit of claim 13, wherein the pharmaceutical is epinephrine, diphenhydramine, or methyl prednisolone.

15. The kit of claim 11, further comprising at least one pharmaceutical for treating local reactions to the microfluidized lysate preparation.

16. The kit of claim 15, wherein the pharmaceutical is hydrocortisone, hydrocortisone cream, acetaminophen, or diphenhydramine.

17. An antibody raised against the microfluidized lysate preparation of claim 4.

18. A vaccine comprising the microfluidized lysate preparation of claim 4.

19. A method of determining whether a subject has been exposed to a given *Leishmania* parasite comprising administering to the subject a panel of antigenic compositions

comprising a plurality of microfluidized lysate preparations prepared from a plurality of *Leishmania* parasites and detecting a presence of an immunogenic reaction that is characteristic to exposure to the given *Leishmania* parasite.

20. The method of claim 19, wherein the plurality of *Leishmania* parasites comprises at least one parasite from the group consisting of *L. tropica, L. mexicana, L. guyanensis, L. braziliensis, L. major, L. donovani, L. chagasi, L. amazonensis, L. peruviana, L. panamensis, L. pifanoi, L. infantum,* and *L. aethiopica.*

21. A method of immunizing a subject against Leishmaniasis comprising administering to the subject an immunogenic amount of the microfluidized lysate preparation of claim 4.

22. A pharmaceutical composition comprising the microfluidized lysate preparation of claim 4 and a pharmaceutically acceptable stabilizer.

23. The pharmaceutical composition of claim 22, wherein the pharmaceutically acceptable stabilizer is phenol.

24. The pharmaceutical composition of claim 22, wherein the composition is in the form of a liquid.

25. The pharmaceutical composition of claim 22, wherein the composition may be frozen or freeze-dried.

26. A method for determining post infection of cutaneous leishmaniasis, mucocutaneous leishmaniasis, or post-kala-azar dermal leishmaniasis in a subject comprising administering to the subject an antigenic amount of at least one microfluidized lysate preparation of claim 4 and observing any immunogenic response to the microfluidized lysate preparation.

27. A method for epidemiologically diagnosing cutaneous leishmaniasis, mucocutaneous leishmaniasis, or post-kala-azar dermal leishmaniasis in a subject comprising

administering to the subject an antigenic amount of at least one microfluidized lysate preparation of claim 4 and observing any immunogenic response to the microfluidized lysate preparation.

28. A method for determining the pattern of present and past leishmaniasis in a subject comprising administering to the subject an antigenic amount of at least one microfluidized lysate preparation of claim 4 and observing any immunogenic response to the microfluidized lysate preparation.

MICROFLUIDIZED LEISHMANIA ANTIGEN AND METHODS OF MAKING AND USING THEREOF

ABSTRACT

Disclosed herein are microfluidized lysate preparations of *Leishmania* parasites and methods of making thereof. Also disclosed are methods of using the microfluidized lysate preparations in skin test antigen assays as well as kits comprising the microfluidized lysate preparations. The microfluidized lysate preparations are made under current good manufacturing practice and may therefore be standardized and such preparations may be produced with consistently.

Shahnan. Shah
09/975020

-key terms

FILE 'HCAPLUS' ENTERED AT 11:41:59 ON 08 MAY 2003

L22 7054 SEA FILE=HCAPLUS ABB=ON PLU=ON LEISHMAN? OR (LEISHMAN? OR L)(W)(TROPICA OR MEXICAN? OR GUYANEN? OR BRAZIL? OR MAJOR OR DONOVAN? OR CHAGASI OR AMAZONEN? OR PERUVIAN? OR PANAMEN? OR PIFANOI OR INFANTUM OR AETHIOPIC?)

L23 1 SEA FILE=HCAPLUS ABB=ON PLU=ON L22 AND (?FLUIDIS? OR ?FLUIDIZ?)

L22 7054 SEA FILE=HCAPLUS ABB=ON PLU=ON LEISHMAN? OR (LEISHMAN? OR L)(W)(TROPICA OR MEXICAN? OR GUYANEN? OR BRAZIL? OR MAJOR OR DONOVAN? OR CHAGASI OR AMAZONEN? OR PERUVIAN? OR PANAMEN? OR PIFANOI OR INFANTUM OR AETHIOPIC?)

L24 302 SEA FILE=HCAPLUS ABB=ON PLU=ON L22 AND (HEAT? OR THERMAL?)

L25 9 SEA FILE=HCAPLUS ABB=ON PLU=ON L24 AND (LYSATE OR SLURR?)

L26 9 L23 OR L25

L26 ANSWER 1 OF 9 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2003:300426 HCAPLUS

TITLE: **Microfluidized Leishmania lysate** prepn. methods and uses thereof

INVENTOR(S): Magill, Alan J.; Stiteler, John M.; Grogl, Max; Rowton, Edgar D.; Eckels, Kenneth H.; Ballou, William R.

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 11 pp.
CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003072714	A1	20030417	US 2001-975020	20011012
WO 2003033533	A1	20030424	WO 2001-US31894	20011012

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-975020 A 20011012

AB Disclosed is the method for prepn. of **microfluidized Leishmania** parasite **lysate**, in particular as it relates to use of the prepns. for assays and immunogenic compns. Also disclosed are methods of using the **microfluidized lysate** prepns. in skin test antigen assays as well as kits comprising the **microfluidized lysate** prepns.

The specific examples include the process for making **L. guyanensis microfluidized lysate**; prodn. of **heat**-treated **L. mexicana** skin test injectable; skin test antigen assay in small group of human subjects; and **heat**-treated **Leishmania** skin test injectable study in a larger group of patients including disease active subjects, healthy **leishmania** subjects, and healed **leishmania** subjects. The **microfluidized lysate** prepns. are made under current good manufg. practice and may therefore be standardized and such prepns. may be produced with consistency.

L26 ANSWER 2 OF 9 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:915724 HCAPLUS
DOCUMENT NUMBER: 138:251243
TITLE: Prostaglandin production from arachidonic acid and evidence for a 9,11-endoperoxide prostaglandin H2 reductase in **Leishmania**
AUTHOR(S): Kabututu, Zakayi; Martin, Samuel K.; Nozaki, Tomoyoshi; Kawazu, Shin-ichiro; Okada, Tetsuya; Munday, Craig Joe; Duszenko, Michael; Lazarus, Michael; Thuita, Lucy W.; Urade, Yoshihiro; Kubata, Bruno Kilunga
CORPORATE SOURCE: Department of Molecular Behavioral Biology, Osaka Bioscience Institute, Suita, Osaka, 565-0874, Japan
SOURCE: International Journal for Parasitology (2002), 32(14), 1693-1700
CODEN: IJPYBT; ISSN: 0020-7519
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB **Lysates** of **Leishmania** promastigotes can metabolize arachidonic acid to prostaglandins. Prostaglandin prodn. was **heat** sensitive and not inhibited by aspirin or indomethacin. We cloned and sequenced the cDNA of **Leishmania major**, **Leishmania donovani**, and **Leishmania tropica** prostaglandin F2.alpha. synthase, and overexpressed their resp. 34-kDa recombinant proteins that catalyze the redn. of 9,11-endoperoxide PGH2 to PGF2.alpha.. Database search and sequence alignment alignment showed that **L. major** prostaglandin F2.alpha. synthase exhibits 61, 99.3, and 99.3% identity with Trypanosoma brucei, **L. donovani**, and **L. tropica** prostaglandin F2.alpha. synthase, resp. Using polymerase chain reaction amplification, Western blotting, and immunofluorescence, we have demonstrated that prostaglandin F2.alpha. synthase protein and gene are present in Old World and absent in New World **Leishmania**, and that this protein is localized to the promastigote cytosol.
REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 3 OF 9 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:633166 HCAPLUS
DOCUMENT NUMBER: 127:328722
TITLE: Molecular characterization of the **heat**

-inducible LmSTI1 protein of **Leishmania major**

AUTHOR(S): Webb, John R.; Campos-Neto, Antonio; Skeiky, Yasir A. W.; Reed, Steven G.

CORPORATE SOURCE: Infectious Disease Research Institute, 1124 Columbia St., Suite 464, Seattle, WA, 98104, USA

SOURCE: Molecular and Biochemical Parasitology (1997), 89(2), 179-193
CODEN: MBIPDP; ISSN: 0166-6851

PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We have recently isolated a cDNA encoding the **Leishmania major** homolog of the yeast stress-inducible protein STI1. Southern blot analyses indicates that this protein is encoded by a single copy gene in **L. major** and that this gene is highly conserved throughout the **Leishmania** genus. The STI1 gene is constitutively expressed in both **L. major** promastigotes and amastigotes however, STI1 transcript levels can be upregulated in promastigotes by a shift in culture temp. from 26 to 37.degree.C. Upregulation of transcript was detectable within 5' of **heat** shock and continued to increase for a further 8 h before returning to constitutive levels. In addn., biosynthetic incorporation of [35S]methionine followed by immunopptn. revealed an increase in the level of nascent STI1 protein synthesized when promastigote cultures were shifted from 26 to 37.degree.C. The **L. major** STI1 protein and the **heat** shock proteins Hsp83 and Hsp70 form a salt-sensitive complex in **L. major** promastigotes as evidenced by co-immunopptn. using an antiserum specific for **L. major** STI1. Furthermore, this complex can be reconstituted in vitro by adding recombinant STI1 contg. an amino-terminal histidine tag to promastigote **lysate** and subsequent purifn. using metal chelate affinity chromatog.

L26 ANSWER 4 OF 9 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1997:539376 HCAPLUS
DOCUMENT NUMBER: 127:275069

TITLE: Detection of lectin activity in **Leishmania** promastigotes and amastigotes

AUTHOR(S): Svobodova, Milena; Bates, Paul A.; Volf, Petr

CORPORATE SOURCE: Department of Parasitology, Faculty of Science, Charles University, Vinicna7, Prague, 12844, Czech.

SOURCE: Acta Tropica (1997), 68(1), 23-35
CODEN: ACTRAQ; ISSN: 0001-706X

PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Cell **lysates** from 16 strains of eight **Leishmania** species were used to test hemagglutination activity (HA) against a variety of RBC. HA was detected using native or neuraminidase-treated rabbit RBC; it was found in promastigotes of all the **Leishmania** strains tested and in axenic amastigotes of **L. mexicana**. The HA was trypsin-sensitive, **heat**-resistant and partially dependent on divalent cations. The HA was inhibited by amino-sugars, LPS from Escherichia coli K 235, fetuin and heparin. The HA is probably

located on the surface of promastigotes, as shown by the same sugar-binding specificity when live cells were used in inhibition tests. **Leishmania** promastigotes were agglutinated with neoglycoproteins NAc-glc-BSA and NAc-gal-BSA. This agglutination was blocked by galactosamine, glucosamine and sialic acid, but not by glcNAc or galNAc. The level of HA is increased in axenic amastigotes when compared to promastigotes. In general, HA was found at a higher titer in infective compared to uninfective strains of **Leishmania**. These results suggest that the hemagglutinin could play a role in the vertebrate phase of the parasite life cycle, possibly in macrophage attachment or invasion.

L26 ANSWER 5 OF 9 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:409831 HCAPLUS
DOCUMENT NUMBER: 127:78733
TITLE: Carbohydrate-binding specificities and physico-chemical properties of lectins in various tissue of phlebotominae sandflies
AUTHOR(S): Palanova, Lucie; Volf, Petr
CORPORATE SOURCE: Department of Parasitology, Charles University, Prague, 128 44/2, Czech Rep.
SOURCE: Folia Parasitologica (Prague) (1997), 44(1), 71-76
CODEN: FPARA9; ISSN: 0015-5683
PUBLISHER: Academy of Sciences of the Czech Republic, Institute of Parasitology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Physico-chem. properties and carbohydrate-binding specificity of hemagglutination activity (HA) were compared in tissue **lysates** and hemolymph of unfed and bloodfed females of five sandfly species. Sandfly gut lectins were found to be **heat** -labile, sensitive to dithiothreitol treatment, freezing/thawing procedures and were affected by divalent cations. The pH optimum of HA ranged between 7.0-7.5. Specificity of gut HA of all species studied was directed towards amino sugars and some glycoconjugates, mainly lipopolysaccharide from Escherichia coli K-235, heparin and fetuin. Gut HA of Phlebotomus papatasi (Scopoli, 1786) was strongly inhibited by lipophosphoglycan (LPG) from **Leishmania major** promastigotes. In females that took blood, the HA was higher but the carbohydrate-binding specificity remained the same; this suggests that the same lectin mol. was present, at different levels, both in unfed and fed flies. High HA was found in ovaries of fed females of Lutzomyia longipalpis (Lutz et Nieva, 1912), P. papatasi and P. duboscqi (Neveu-Lemaire, 1906). In P. papatasi and P. duboscqi the HA was present also in the hemolymph and head **lysates** of both fed and unfed females. Carbohydrate-binding specificity of HA present in these tissues was similar with the gut lectin.

L26 ANSWER 6 OF 9 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1996:125201 HCAPLUS
DOCUMENT NUMBER: 124:199873
TITLE: Recombinant **Leishmania donovani heat** shock protein 70 is recognized by T cells from immune individuals
AUTHOR(S): Arora, Sunil K.; Sehgal, Shobha; Tryon, Victor V.; Melby, Peter C.

CORPORATE SOURCE: Department Immunopathology, Postgraduate Institute Medical Education and Research, Chandigarh, 160012, India
SOURCE: Immunology & Infectious Diseases (1995), 5(4), 282-6
CODEN: IINDEK; ISSN: 0959-4957
PUBLISHER: Rapid Science Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The acquisition of immunity to re-infection following cure of **leishmaniasis** suggests that vaccination could play a role in the control of this disease. T-cell responses are of primary importance in the acquisition of immunity, but the **leishmanial** antigens which elicit these responses in immune humans have not been defined. The goal of the present study was to identify recombinant **Leishmania donovani** antigens which stimulate human T-cell responses. Sero-reactive clones were identified from an **L. donovani** cDNA library by screening with patient sera, and assayed for their ability to stimulate peripheral blood lymphocytes obtained from immune individuals using a T-cell blotting technique. A bacterial **lysate** contg. an expressed 70 kDa fusion protein was found to induce a lymphoproliferative response, and this response was confirmed with the purified recombinant fusion protein. Nucleotide sequencing of the cDNA encoding this T-cell antigen revealed that it was **heat** shock protein 70.

L26 ANSWER 7 OF 9 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1994:553071 HCAPLUS
DOCUMENT NUMBER: 121:153071
TITLE: Proteinase activities during temperature-induced stage differentiation of species complexes of **Leishmania**
AUTHOR(S): Leon, Leonor L.; Temporal, Rosane M.; Soares, Maurilio J.; Grimaldi, Gabriel Jr.
CORPORATE SOURCE: Dep. de Imunol., Inst. Oswaldo Cruz, Rio de Janeiro, 21405-900, Brazil
SOURCE: Acta Tropica (1994), 56(4), 289-98
CODEN: ACTRAQ; ISSN: 0001-706X
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The authors examd. by SDS-PAGE, using gelatin, bovine serum albumin, or human IgG as substrate, proteinase activities in cell **lysates** from selected species complexes of **Leishmania**. The inhibition of proteinase activity caused by L-trans-epoxysuccinylleucylamido (4-guanidino) butane (E-64), which is known to act only on cysteinyl proteinases, revealed a 31 kDa component of this class of enzymes in sol., but not in membrane-enriched prepns., of either **L. amazonensis** or **L. major**-like parasites from the New World. The proteinase component was detectable in the **leishmanial** multiplicative promastigote stage (log phase), and its concn. apparently increased during the **thermally** induced transformation of promastigotes to amastigote-like forms in vitro. Comparative studies revealed that taxonomically distinct species complexes of **Leishmania** possess high amastigote cysteine proteinase activity. This feature, however, was lacking in other developmental stages of the species (**L.**

braziliensis, L. chagasi, L. aethiopica, and **L. donovani**) analyzed. Furthermore, lesion amastigotes of **L. amazonensis** displayed ultrastructurally recognizable megasomes, but megasome-like or large multivesicular body organelles could be detected only in axenic amastigotes of both **L. amazonensis** and **L. major**-like species.

L26 ANSWER 8 OF 9 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1994:29180 HCAPLUS
DOCUMENT NUMBER: 120:29180
TITLE: Antigen-reactive .gamma..delta. T cells in human **leishmaniasis**
AUTHOR(S): Russo, Donna M.; Armitage, Richard J.; Barral-Netto, Manoel; Barral, Aldina; Grabstein, Kenneth H.; Reed, Steven G.
CORPORATE SOURCE: Seattle Biomed. Res. Inst., Seattle, WA, 98109, USA
SOURCE: Journal of Immunology (1993), 151(7), 3712-18
CODEN: JOIMA3; ISSN: 0022-1767
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In the present study the expression of .gamma..delta. TCR on T lymphocytes from patients with cutaneous, mucosal, or visceral **leishmaniasis** was examd. All of these patient groups had elevated levels of .gamma..delta. T cells in peripheral blood. The percentage of T cells expressing .gamma..delta. TCR was increased significantly by stimulation in vitro with certain parasite antigens (Ag). T-cell lines generated by stimulation with promastigote **lysates** of **Leishmania amazonensis** or L. brasiliensis typically contained 25-60% .gamma..delta. T cells. In contrast, 2 immunodominant surface Ag of **L. amazonensis**, gp63 and gp42, did not expand .gamma..delta. T cells from infected patients, although both Ag elicited strong .alpha..beta. T-cell responses. .gamma..delta. T cells isolated from a **Leishmania**-specific T-cell line responded to stimulation with promastigote **lysate**. Of particular interest, .gamma..delta. T cells from PBMC of a patient with mucosal **leishmaniasis** responded to stimulation with a recombinant 70 kDa **heat** shock protein of **L. chagasi**. Thus, several clin. forms of **leishmaniasis** induced elevated nos. of .gamma..delta. T cells that responded specifically to **Leishmania** Ag in vitro. This component of the T-cell response to **Leishmania** may therefore impact the outcome of clin. disease.

L26 ANSWER 9 OF 9 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1993:447030 HCAPLUS
DOCUMENT NUMBER: 119:47030
TITLE: **Leishmania major**-specific, CD4+, major histocompatibility complex class II-restricted T cells derived in vitro from lymphoid tissues of naive mice
AUTHOR(S): Shankar, Anuraj H.; Titus, Richard G.
CORPORATE SOURCE: Dep. Trop. Public Health, Harvard Sch. Public Health, Boston, MA, 02115, USA
SOURCE: Journal of Experimental Medicine (1993), 178(1), 101-11

CODEN: JEMEAV; ISSN: 0022-1007
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Several studies indicate that the outcome of exptl. murine cutaneous **leishmaniasis** caused by **Leishmania major** (Lm) is detd. by immunol. events occurring shortly after infection. These events lead to outgrowth of either protective CD4+ T cells in the C57BL/6 mouse, which cures, or exacerbative cells in the BALB/c mouse, which succumbs to disease. Potential factors influencing the outgrowth of protective or exacerbative T cells include antigen-presenting cells (APC), cytokines, and parasite antigens. An in vitro system, in which one could precisely control the factors shaping early events in the T cell response to Lm, would be very useful. To this end, the authors examd. the the vitro response of naive lymphocytes to Lm promastigotes. The data presented here show that Lm-specific CD4+ TCR .alpha./.beta.+ T cells can be generated in vitro from spleen and lymph node cell populations of naive mice. Furthermore, they can be obtained from the CD44low (unprimed) population of T lymphocytes, indicating that in vitro priming occurs. The ability to generate these T cells is dependent on the presence of live parasites and is not due to a parasite-derived nonspecific T cell mitogen. Restimulation, as assayed by proliferation, requires APC bearing syngeneic I-A. Optimal restimulation of the in vitro derived T cells is achieved only when live promastigotes are used. The T cells do not proliferate in response to a frozen-and-thawed **lysate** of promastigotes, yet they exhibit mild reactivity to **lysates** prepd. from **heat**-shocked promastigotes. Furthermore, they do not recognize two predominant antigens on the promastigote surface, lipophosphoglycan and gp63. T cells derived in vitro with Lm show crossreactivity with live **L. donovani**, less crossreactivity with live **L. mexicana**, and no crossreactivity with live Bacillus-Calmette-Guerin or live Brugia malayi microfilariae. Finally, these early T cells, whether derived from healing C57BL/6 or non-healing BALB/c mice, produce interleukin 2 (IL-2), IL-4, and interferon .gamma..

(FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO' ENTERED AT 11:44:30 ON 08 MAY 2003)

L27 3 S L23
L28 39 S L25
L29 41 S L27 OR L28
L30 19 DUP REM L29 (22 DUPLICATES REMOVED)

L30 ANSWER 1 OF 19 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2003120363 IN-PROCESS
DOCUMENT NUMBER: 22521108 PubMed ID: 12633659
TITLE: Prostaglandin production from arachidonic acid and evidence for a 9,11-endoperoxide prostaglandin H(2) reductase in **Leishmania**.
AUTHOR: Kabututu Zakayi; Martin Samuel K; Nozaki Tomoyoshi; Kawazu Shin ichiro; Okada Tetsuya; Munday Craig Joe; Duszenko Michael; Lazarus Michael; Thuita Lucy W; Urade Yoshihiro; Kubata Bruno Kilunga
CORPORATE SOURCE: Department of Molecular Behavioral Biology, Osaka Bioscience Institute, Suita, 565-0874, Osaka, Japan.
SOURCE: INTERNATIONAL JOURNAL FOR PARASITOLOGY, (2003 Feb) 33 (2) 221-8.

Journal code: 0314024. ISSN: 0020-7519.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20030314
Last Updated on STN: 20030314

AB **Lysates** of **Leishmania** promastigotes can metabolise arachidonic acid to prostaglandins. Prostaglandin production was **heat** sensitive and not inhibited by aspirin or indomethacin. We cloned and sequenced the cDNA of **Leishmania major**, **Leishmania donovani**, and **Leishmania tropica** prostaglandin F(2alpha) synthase, and overexpressed their respective 34-kDa recombinant proteins that catalyse the reduction of 9,11-endoperoxide PGH(2) to PGF(2alpha). Database search and sequence alignment showed that **L. major** prostaglandin F(2alpha) synthase exhibits 61, 99.3, and 99.3% identity with Trypanosoma brucei, **L. donovani**, and **L. tropica** prostaglandin F(2alpha) synthase, respectively. Using polymerase chain reaction amplification, Western blotting, and immunofluorescence, we have demonstrated that prostaglandin F(2alpha) synthase protein and gene are present in Old World and absent in New World **Leishmania**, and that this protein is localised to the promastigote cytosol.

L30 ANSWER 2 OF 19 SCISEARCH COPYRIGHT 2003 THOMSON ISI
ACCESSION NUMBER: 2003:277467 SCISEARCH
THE GENUINE ARTICLE: 658FN
TITLE: Prostaglandin production from arachidonic acid and evidence for a 9,11-endoperoxide prostaglandin H-2 reductase in **Leishmania** (vol 32, pg 1693, 2002)
AUTHOR: Kabututu Z; Martin S K; Nozaki T; Kawazu S; Okada T; Munday C J; Duszenko M; Lazarus M; Wangari L W; Urade Y; Kubata B K (Reprint)
CORPORATE SOURCE: Osaka Biosci Inst, Dept Mol Behav Biol, Suita, Osaka 5650874, Japan (Reprint); United Stores Army Med Res Unit Kenya, Unit 64109, APO, AE 09831 USA; Natl Inst Infect Dis, Dept Parasitol, Shinjuku Ku, Tokyo 1628640, Japan; Int Med Ctr Japan, Res Inst, Shinjuku Ku, Tokyo 1628655, Japan; Osaka Univ, Sch Hlth & Sport Sci, Dept Med Sci 3, Toyonaka, Osaka 5600043, Japan; Univ Tubingen, Inst Physiol Chem, D-72076 Tubingen, Germany; Georgetown Univ, Dept Biol, Washington, DC 20057 USA
COUNTRY OF AUTHOR: Japan; USA; Germany
SOURCE: INTERNATIONAL JOURNAL FOR PARASITOLOGY, (FEB 2003) Vol. 33, No. 2, pp. 219-+.
Publisher: PERGAMON-ELSEVIER SCIENCE LTD, THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, ENGLAND.
ISSN: 0020-7519.
DOCUMENT TYPE: Errata; Journal
LANGUAGE: English
REFERENCE COUNT: 36
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB **Lysates** of **Leishmania** promastigotes can

metabolise arachidonic acid to prostaglandins. Prostaglandin production was **heat** sensitive and not inhibited by aspirin or indomethacin. We cloned and sequenced the cDNA of **Leishmania major, Leishmania donovani**, and **Leishmania tropica** prostaglandin F-2alpha synthase, and overexpressed their respective 34-kDa recombinant proteins that catalyse the reduction of 9,11-endoperoxide PGH(2) to PGF(2alpha). Database search and sequence alignment showed that **L. major** prostaglandin F-2alpha synthase exhibits 61, 99.3, and 99.3% identity with Trypanosoma brucei, **L. donovani**, and **L. tropica** prostaglandin F-2alpha synthase, respectively. Using polymerase chain reaction amplification, Western blotting, and immunofluorescence, we have demonstrated that prostaglandin F-2alpha synthase protein and gene are present in Old World and absent in New World **Leishmania**, and that this protein is localised to the promastigote cytosol.

L30 ANSWER 3 OF 19 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 2002-479611 [51] WPIDS
DOC. NO. CPI: C2002-136458
TITLE: Inducing an immune response in a subject against a type of cancer or a pathogen by administering a composition comprising unfractionated cellular proteins obtained from cancer cells or cells with antigenicity of the pathogen.
DERWENT CLASS: B04 D16
INVENTOR(S): SRIVASTAVA, P K
PATENT ASSIGNEE(S): (UYCO-N) UNIV CONNECTICUT HEALTH CENT
COUNTRY COUNT: 23
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002030434	A1	20020418	(200251)*	EN	77
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR					
W: AU CA JP US					
AU 2001094560	A	20020422	(200254)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002030434	A1	WO 2001-US28841	20010917
AU 2001094560	A	AU 2001-94560	20010917

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2001094560	A Based on	WO 200230434

PRIORITY APPLN. INFO: US 2000-233174P 20000915
AN 2002-479611 [51] WPIDS
AB WO 200230434 A UPAB: 20020812
NOVELTY - Inducing (M2) an immune response in a subject against

cancer or a pathogen, or treating or preventing cancer or an infection by a pathogen, involving administering a composition (I) comprising unfractionated cellular proteins (UCP) obtained from cells of the type of cancer or its metastasis; or cells with an antigenicity of the pathogen, respectively, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) preparing (M1) a vaccine for treatment or prevention of cancer involves lysing cancer cells to produce a crude cell **lysate**; and centrifuging the crude cell **lysate** or supernatant derived from the cancer cells one or more times to remove intact cells, where there is substantially no subjecting of cellular proteins within the **lysate** to any method that selectively removes soluble proteins;

(2) treating or preventing a type of cancer by administering to a subject in need of such treatment or prevention, a composition comprising unfractionated cytosolic soluble proteins obtained from cells transformed with an expressing nucleic acid encoding a molecule displaying antigenicity of a tumor-associated antigen or tumor-specific antigen of the type of cancer;

(3) a kit (K1) comprising in one or more containers (for treatment or prevention of a type of cancer) UCP obtained from cells of the type of cancer or its metastasis or from cells transformed with and expressing a nucleic acid encoding a molecule displaying antigenicity of a tumor-associated antigen or tumor-specific antigen of the type of cancer; and

(4) a kit (K2) comprising in one or more containers (for treatment or prevention of an infectious disease) UCP obtained from cells with an antigenicity of a pathogen that causes the infectious disease.

ACTIVITY - Cytostatic; Antibacterial; Virucide; Anti-HIV.

The ability of compositions comprising unfractionated cellular proteins derived from meth A tumor cells to induce regression of Meth A tumors in vivo was tested. A total of 7 groups, with each group consisting of 10 female BALB/c mice weighing approx. 25 g each, were used. In each set, mice were injected intradermally with 105 Meth A cells. Beginning 5 days after injection of the tumor cells (day 5), each group of mice was administered phosphate buffered saline (PBS) buffer, irradiated whole Meth A tumor cells, 1 multiply 103, 1 multiply 104, 1 multiply 105, 1 multiply 106, or 1 multiply 107 cell equivalents of unfractionated cellular proteins prepared from Meth A tumor cells. These treatments were repeated for each group of mice at day 7, 9, 12, 14 and 16. Average tumor diameter (in mm) was determined daily for each mouse until day 25 and the results indicated that unfractionated cellular proteins isolated from a tumor treatment can be used for treatment of that tumor in vivo.

MECHANISM OF ACTION - Immune response inducer; Vaccine.

USE - M2 is useful for inducing an immune response in a subject against a type of cancer or a pathogen, or treating or preventing a type of cancer or an infection by a pathogen. The method is useful for inducing an immune response against, or for treating or preventing cancer such as sarcoma or carcinoma, such as fibrosarcoma, myxosarcoma, liposarcoma, chondrosarcoma, osteogenic sarcoma, angiosarcoma, endotheliosarcoma, lymphangiosarcoma, lymphangioendotheliosarcoma, synovioma, mesothelioma, Ewing's tumor, leiomyosarcoma, rhabdomyosarcoma, colon carcinoma, pancreatic cancer, breast cancer, ovarian cancer, prostate cancer, squamous

cell carcinoma, basal cell carcinoma, adenocarcinoma, sweat gland carcinoma, sebaceous gland carcinoma, papillary carcinoma, papillary adenocarcinomas and cystadenocarcinoma, in a subject, preferably human. The method is also useful for inducing an immune response against a pathogen and for treating or preventing an infection by a pathogen such as hepatitis virus type A, B, C, influenza virus, varicella virus, adenovirus, herpes simplex virus type I (HSV-I), herpes simplex virus type II (HSV-II), rinderpest virus, rhinovirus, echovirus, rotavirus, respiratory syncytial virus, papilloma virus, papova virus, cytomegalovirus, echinovirus, arbovirus, hantavirus, coxsackie virus, mumps virus, measles virus, rubella virus, polio virus, human immunodeficiency virus type I (HIV-I), HIV-II, Mycobacteria rickettsia, Mycoplasma, Neisseria, Legionella, **Leishmania**, Kokzidioa, Trypanosoma, Chlamydia, or Rickettsia in a subject preferably, human (all claimed).
Dwg.0/0

L30 ANSWER 4 OF 19 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 2002702927 IN-PROCESS
DOCUMENT NUMBER: 22352101 PubMed ID: 12464415
TITLE: Prostaglandin production from arachidonic acid and evidence for a 9,11-endoperoxide prostaglandin H(2) reductase in **Leishmania**.
AUTHOR: Kabututu Zakayi; Martin Samuel K; Nozaki Tomoyoshi; Kawazu Shin ichiro; Okada Tetsuya; Munday Craig Joe; Duszenko Michael; Lazarus Michael; Thuita Lucy W; Urade Yoshihiro; Kubata Bruno Kilunga
CORPORATE SOURCE: Department of Molecular Behavioral Biology, Osaka Bioscience Institute, Suita, 565-0874, Osaka, Japan.
SOURCE: INTERNATIONAL JOURNAL FOR PARASITOLOGY, (2002 Dec) 32 (14) 1693-700.
Journal code: 0314024. ISSN: 0020-7519.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20021217
Last Updated on STN: 20021217

AB **Lysates** of **Leishmania** promastigotes can metabolise arachidonic acid to prostaglandins. Prostaglandin production was **heat** sensitive and not inhibited by aspirin or indomethacin. We cloned and sequenced the cDNA of **Leishmania major**, **Leishmania donovani**, and **Leishmania tropica** prostaglandin F(2alpha) synthase, and overexpressed their respective 34-kDa recombinant proteins that catalyse the reduction of 9,11-endoperoxide PGH(2) to PGF(2alpha). Database search and sequence alignment alignment showed that **L. major** prostaglandin F(2alpha) synthase exhibits 61, 99.3, and 99.3% identity with Trypanosoma brucei, **L. donovani**, and **L. tropica** prostaglandin F(2alpha) synthase, respectively. Using polymerase chain reaction amplification, Western blotting, and immunofluorescence, we have demonstrated that prostaglandin F(2alpha) synthase protein and gene are present in Old World and absent in New World **Leishmania**, and that this protein is localised to the promastigote cytosol.

L30 ANSWER 5 OF 19 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 2001:557605 BIOSIS
DOCUMENT NUMBER: PREV200100557605
TITLE: Selective production of bikaverin in a **fluidized** bioreactor with immobilized Gibberella fujikuroi.
AUTHOR(S): Escamilla-Silva, Eleazar (1); Poggi-Varaldo, Hector; De la Torre-Martinez, M. Mayra; Sanchez Cornejo, M. A. Guadalupe; Dendooven, Luc
CORPORATE SOURCE: (1) Department of Chemistry, Technological Institute of Celaya, Av. Tecnologico y A. Garcia Cubas S/N, Celaya, GTO: eleazar@iqcelaya.itc.mx Mexico
SOURCE: World Journal of Microbiology & Biotechnology, (July, 2001) Vol. 17, No. 5, pp. 469-474. print.
ISSN: 0959-3993.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The best culture medium composition for the production of bikaverin by Gibberella fujikuroi in shake-flasks, i.e. 100 g glucose l-1; 1 g NH4Cl l-1; 2 g rice flour l-1; 5 g KH2PO4 l-1 and 2.5 g MgSO4 l-1, was obtained through a fractional factorial design and then scaled-up to a **fluidized** bioreactor. The effects of carbon and nitrogen concentrations, inoculum size, aeration, flow rate and bead sizes on batch bikaverin production using immobilized G. fujikuroi in a **fluidized** bioreactor were determined by an orthogonal experimental design. Concentrations of up to 6.83 g bikaverin l-1 were obtained when the medium contained 100 g glucose l-1 and 1 g NH4Cl l-1 with an inoculum ratio of 10% v/v, an aeration rate of 3 volumes of air per volume of medium min-1, and a bead size of 3 mm. Based on dry weight, the bikaverin production was 30-100 times larger than found in submerged culture and approximately three times larger than reported for solid substrate fermentation.

L30 ANSWER 6 OF 19 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 2001-015543 [02] WPIDS
DOC. NO. CPI: C2001-004080
TITLE: Stable granular oral antifungal and antiparasitic formulations, obtained by spraying solution containing echinocandin and carbohydrate onto **fluidized** carrier.
DERWENT CLASS: A96 B02 C01 C02
INVENTOR(S): SCHWIER, J R; TAYLOR, J
PATENT ASSIGNEE(S): (ELIL) LILLY & CO ELI; (SCHW-I) SCHWIER J R; (TAYL-I) TAYLOR J
COUNTRY COUNT: 91
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000051567	A1	20000908	(200102)*	EN	40
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW					
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
AU 2000033934	A	20000921	(200102)		
EP 1156784	A1	20011128	(200201)	EN	

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI

BR 2000008713	A	20011226	(200206)
KR 2001112302	A	20011220	(200239)
CN 1345230	A	20020417	(200248)
US 2002151474	A1	20021017	(200270)
JP 2002538097	W	20021112	(200275) 48

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 2000051567	A1		WO 2000-US5547	20000302
AU 2000033934	A		AU 2000-33934	20000302
EP 1156784	A1		EP 2000-912160	20000302
			WO 2000-US5547	20000302
BR 2000008713	A		BR 2000-8713	20000302
			WO 2000-US5547	20000302
KR 2001112302	A		KR 2001-711216	20010903
CN 1345230	A		CN 2000-805698	20000302
US 2002151474	A1	Provisional	US 1999-122693P	19990303
		Cont of	WO 2000-US5547	20000302
			US 2001-942435	20010829
JP 2002538097	W		JP 2000-602036	20000302
			WO 2000-US5547	20000302

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000033934	A	Based on	WO 200051567
EP 1156784	A1	Based on	WO 200051567
BR 2000008713	A	Based on	WO 200051567
JP 2002538097	W	Based on	WO 200051567

PRIORITY APPLN. INFO: US 1999-122693P 19990303; US 2001-942435 20010829

AN 2001-015543 [02] WPIDS

AB WO 200051567 A UPAB: 20020613

NOVELTY - Preparation of an oral pharmaceutical formulation (A) comprises: (a) mixing an echinocandin compound (I) (optionally as a carbohydrate complex), carbohydrate(s) (II) in a solvent (or solvent mixture), (b) spraying the obtained solution weight onto a **fluidized** layer of granular diluent or carrier (III) and (c) removing excess solvent(s) to form granules.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for:

(i) a variant on the process, in which the mixture in (a) further contains a soluble granulating agent (IV) and (III) is replaced by a non-granular diluent or carrier (III');

(ii) (A) obtained by the processes; and

(iii) medicaments comprising (A).

USE - For treating fungal infections (claimed), especially systemic or skin infections by Candida albicans or Aspergillus fumigatus infections. (I) are also effective against organisms causing opportunistic infections in immunosuppressed (e.g. AIDS) patients, such as Pneumonocystis carinii (causing pneumocystis pneumonia); and protozoans such as Plasmodium, **Leishmania**, Trypanosoma, Cryptosporidium, Isospora, Cyclospora, Trichomonas or

Microsporidiosis.
ADVANTAGE - Inclusion of (II) markedly enhances the thermal stability of (I).
Dwg.0/0

L30 ANSWER 7 OF 19 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:14414 BIOSIS
DOCUMENT NUMBER: PREV200100014414
TITLE: ODS **Leishmania** skin test, MFL-LSTA(R2): Stability of the cGMP product in the guinea pig animal model.
AUTHOR(S): Stiteler, J. M. (1); Grogl, M.; Rowton, E. D.
CORPORATE SOURCE: (1) Department of Entomology, Division of Communicable Diseases and Immunology, Walter Reed Army Institute of Research, Washington, DC USA
SOURCE: American Journal of Tropical Medicine and Hygiene, (March, 2000) Vol. 62, No. 3 Supplement, pp. 310. print.
Meeting Info.: 49th Annual Meeting of the American Society of Tropical Medicine and Hygiene Houston, Texas, USA October 29-November 02, 2000 American Society of Tropical Medicine and Hygiene
. ISSN: 0002-9637.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L30 ANSWER 8 OF 19 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 1998030246 MEDLINE
DOCUMENT NUMBER: 98030246 PubMed ID: 9364964
TITLE: Molecular characterization of the **heat** -inducible LmSTI1 protein of **Leishmania major**.
AUTHOR: Webb J R; Campos-Neto A; Skeiky Y A; Reed S G
CORPORATE SOURCE: Infectious Disease Research Institute, Seattle, WA 98104, USA.
CONTRACT NUMBER: AI25038 (NIAID)
SOURCE: MOLECULAR AND BIOCHEMICAL PARASITOLOGY, (1997 Nov) 89 (2) 179-93.
Journal code: 8006324. ISSN: 0166-6851.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199712
ENTRY DATE: Entered STN: 19980109
Last Updated on STN: 19980109
Entered Medline: 19971223

AB We have recently isolated a cDNA encoding the **Leishmania major** homologue of the yeast stress-inducible protein STI1. Southern blot analyses indicate that this protein is encoded by a single copy gene in **L. major** and that this gene is highly conserved throughout the **Leishmania** genus. The STI1 gene is constitutively expressed in both **L. major** promastigotes and amastigotes however, STI1 transcript levels can be upregulated in promastigotes by a shift in culture temperature from 26 to 37 degrees C. Upregulation of transcript was detectable within 5' of **heat** shock and continued to

increase for a further 8 h before returning to constitutive levels. In addition, biosynthetic incorporation of [35S]methionine followed by immunoprecipitation revealed an increase in the level of nascent STI1 protein synthesized when promastigote cultures were shifted from 26 to 37 degrees C. The **L. major** STI1 protein and the **heat** shock proteins Hsp83 and Hsp70 form a salt-sensitive complex in **L. major** promastigotes as evidenced by co-immunoprecipitation using an antiserum specific for **L. major** STI1. Furthermore, this complex can be reconstituted in vitro by adding recombinant STI1 containing an amino-terminal histidine tag to promastigote **lysate** and subsequent purification using metal chelate affinity chromatography.

L30 ANSWER 9 OF 19 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 97331869 MEDLINE
DOCUMENT NUMBER: 97331869 PubMed ID: 9188176
TITLE: Carbohydrate-binding specificities and physico-chemical properties of lectins in various tissue of phlebotominae sandflies.
AUTHOR: Palanova L; Volf P
CORPORATE SOURCE: Department of Parasitology, Charles University, Prague, Czech Republic.
SOURCE: FOLIA PARASITOLOGICA, (1997) 44 (1) 71-6. Journal code: 0065750. ISSN: 0015-5683.
PUB. COUNTRY: Czech Republic
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199707
ENTRY DATE: Entered STN: 19970805
Last Updated on STN: 19970805
Entered Medline: 19970721

AB Physico-chemical properties and carbohydrate-binding specificity of hemagglutination activity (HA) were compared in tissue **lysates** and haemolymph of unfed and bloodfed females of five sandfly species. Sandfly gut lectins were found to be **heat** -labile, sensitive to dithiotreitol treatment, freezing/thawing procedures and were affected by divalent cations. The pH optimum of HA ranged between 7.0-7.5. Specificity of gut HA of all species studied was directed towards aminosugars and some glycoconjugates, mainly lipopolysaccharide from Escherichia coli K-235, heparin and fetuin. Gut HA of Phlebotomus papatasi (Scopoli, 1786) was strongly inhibited by lipophosphoglycan (LPG) from **Leishmania major** promastigotes. In females, that took blood, the HA was higher but the carbohydrate-binding specificity remained the same; this suggests that the same lectin molecule was present, at different levels, both in unfed and fed flies. High HA was found in ovaries of fed females of Lutzomyia longipalpis (Lutz et Nieva, 1912), P. papatasi and P. duboscqi Neveu-Lemaire, 1906. In P. papatasi and P. duboscqi the HA was present also in the haemolymph and head **lysates** of both fed and unfed females. Carbohydrate-binding specificity of HA present in these tissues was similar with the gut lectin.

L30 ANSWER 10 OF 19 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 1998013241 MEDLINE
DOCUMENT NUMBER: 98013241 PubMed ID: 9352000
TITLE: Detection of lectin activity in **Leishmania**

promastigotes and amastigotes.
AUTHOR: Svobodova M; Bates P A; Volf P
CORPORATE SOURCE: Department of Parasitology, Faculty of Science, Charles University, Prague, Czech Republic.. volf@beba.cesnet.cz
SOURCE: ACTA TROPICA, (1997 Oct 14) 68 (1) 23-35. Journal code: 0370374. ISSN: 0001-706X.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199712
ENTRY DATE: Entered STN: 19980109
Last Updated on STN: 19980109
Entered Medline: 19971204

AB Cell **lysates** from 16 strains of eight **Leishmania** species were used to test haemagglutination activity (HA) against a variety of RBC. HA was detected using native or neuraminidase-treated rabbit RBC; it was found in promastigotes of all the **Leishmania** strains tested and in axenic amastigotes of **L. mexicana**. The HA was trypsin-sensitive, **heat**-resistant and partially dependent on divalent cations. The HA was inhibited by amino-sugars, LPS from E. coli K 235, fetuin and heparin. The HA is probably located on the surface of promastigotes, as shown by the same sugar-binding specificity when live cells were used in inhibition tests. **Leishmania** promastigotes were agglutinated with neoglycoproteins NAc-glc-BSA and NAc-gal-BSA. This agglutination was blocked by galactosamine, glucosamine and sialic acid, but not by glcNAc or galNAc. The level of HA is increased in axenic amastigotes when compared to promastigotes. In general, HA was found at a higher titre in infective compared to uninfective strains of **Leishmania**. These results suggest that the haemagglutinin could play a role in the vertebrate phase of the parasite life cycle, possibly in macrophage attachment or invasion.

L30 ANSWER 11 OF 19 SCISEARCH COPYRIGHT 2003 THOMSON ISI
ACCESSION NUMBER: 96:881739 SCISEARCH
THE GENUINE ARTICLE: VU501
TITLE: Molecular cloning of a novel protein antigen of **Leishmania major** that elicits a potent immune response in experimental murine **leishmaniasis**
AUTHOR: Webb J R; Kaufmann D; Camposneto A; Reed S G (Reprint)
CORPORATE SOURCE: INFECT DIS RES INST, 1124 COLUMBIA ST, SUITE 464, SEATTLE, WA 98104 (Reprint); INFECT DIS RES INST, SEATTLE, WA 98104; CORNELL UNIV, COLL MED, NEW YORK, NY 10021; CORIXA CORP, SEATTLE, WA 98104
COUNTRY OF AUTHOR: USA
SOURCE: JOURNAL OF IMMUNOLOGY, (1 DEC 1996) Vol. 157, No. 11, pp. 5034-5041. Publisher: AMER ASSOC IMMUNOLOGISTS, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814. ISSN: 0022-1767.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English

REFERENCE COUNT: 40

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB BALB/c mice are highly susceptible to infection with the protozoan parasite **Leishmania major**. This susceptibility has been attributed, in part, to the expansion of parasite-specific CD4(+) Th2 cells that antagonize Th1 responses and promote humoral immunity. In the present study, we have utilized sera from **L. major**-infected BALB/c mice to screen an **L, major** amastigote cDNA expression library. One of the clones detected encodes a novel Ag designated as **L. major** stress-inducible 1 (LmSTI1). LmSTI1 contains six copies of the tetratricopeptide consensus motif and is highly related to a family of stress-inducible proteins that is conserved from yeast to humans. Sera from **L. major** -infected BALB/c mice have LmSTI1-specific Ab titers in excess of 1:200,000, comprised predominantly of IgG1, IgG2A, and IgC2B isotypes. Recombinant LmSTI1 protein elicited strong proliferative responses from draining lymph node cells of **L. major**-infected BALB/c mice at both early (10 days) and late (28 days) stages of infection and elicited production of high levels of IFN-gamma and low levels of IL-4. In contrast, soluble **leishmanial lysate** elicited high levels of IL-4 and low IFN-gamma production. Thus, we have identified an Ag of **Leishmania** capable of eliciting a mixed cellular response that is skewed toward a Th1 phenotype in susceptible BALB/c mice with advanced infections. In addition, analyses of sera from human patients with cutaneous, visceral, and post-kala azar visceral **leishmaniasis** indicated that a majority of individuals from all three clinical groups mounted strong humoral responses against LmSTI1.

L30 ANSWER 12 OF 19 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1996:127968 BIOSIS
DOCUMENT NUMBER: PREV199698700103
TITLE: Recombinant **Leishmania donovani** **heat** shock protein 70 is recognized by T cells from immune individuals.
AUTHOR(S): Arora, Sunil K.; Sehgal, Shobha; Tryon, Victor V.; Melby, Peter C. (1)
CORPORATE SOURCE: (1) Dep. Med., Div. Infectious Diseases, Univ. Tex. Health Sci. Cent., 7703 Floyd Curl Drive, San Antonio, TX 78284-7881 USA
SOURCE: Immunology & Infectious Diseases (Oxford), (1995) Vol. 5, .No. 4, pp. 282-286. ISSN: 0959-4957.
DOCUMENT TYPE: Article
LANGUAGE: English

AB The acquisition of immunity to re-infection following cure of **leishmaniasis** suggests that vaccination could play a role in the control of the disease. T-cell responses are of primary importance in the acquisition of immunity, but the **leishmanial** antigens which elict these responses in immune humans have not been defined. The goal of the present study was to identify recombinant **Leishmania donovani** antigens which stimulate human T-cell responses. Sero-reactive clones were identified from an **L. donovani** cDNA library by screening with patient sera, and assayed for their ability to stimulate peripheral blood lymphocytes obtained from

immune individuals using a T-cell blotting technique. A bacterial **lysate** containing an expressed 70 kDa fusion protein was found to induce a lymphoproliferative response, and this response was confirmed with the purified recombinant fusion protein. Nucleotide sequencing of the cDNA encoding this T-cell antigen revealed that it was **heat** shock protein 70.

L30 ANSWER 13 OF 19 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 94295477 MEDLINE
DOCUMENT NUMBER: 94295477 PubMed ID: 8023752
TITLE: Proteinase activities during temperature-induced stage differentiation of species complexes of **Leishmania**.
AUTHOR: Leon L L; Temporal R M; Soares M J; Grimaldi Junior G
CORPORATE SOURCE: Departamento de Imunologia, Instituto Oswaldo Cruz, Rio de Janeiro, Brazil.
SOURCE: ACTA TROPICA, (1994 Apr) 56 (4) 289-98.
Journal code: 0370374. ISSN: 0001-706X.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199408
ENTRY DATE: Entered STN: 19940815
Last Updated on STN: 20000303
Entered Medline: 19940802

AB We have examined by sodium dodecyl sulphate-polyacrylamide gel electrophoresis (SDS-PAGE), using gelatin, bovine serum albumin (BSA) or human IgG as substrate, proteinase activities in cell **lysates** from selected species complexes of **Leishmania**. The inhibition of proteinase activity caused by the reagent L-trans-epoxysuccinylleucylamido(4-guanidino)butane (E-64), which is known to act only on cysteinyl proteinases, revealed a 31 kDa component of this class of enzymes in soluble, but not in membrane-enriched preparations, of either **L. amazonensis** or **L. major**-like parasites from the New World. The proteinase component was detectable in the **leishmanial** multiplicative promastigote stage (log phase) and its concentration apparently increased during the **thermally** induced transformation of promastigotes to amastigote-like forms in vitro. Comparative studies revealed that taxonomically distinct species complexes of **Leishmania** possess high amastigote cysteine proteinase activity. This feature, however, was lacking in other developmental stages of the species (**L. braziliensis**, **L. chagasi**, **L. aethiopica**, and **L. donovani**) analyzed. Furthermore, lesion amastigotes of **L. amazonensis** displayed ultrastructurally recognizable megasomes, but megasome-like or large multivesicular body organelles could be detected only in axenic amastigotes of both **L. amazonensis** and **L. major**-like species.

L30 ANSWER 14 OF 19 MEDLINE DUPLICATE 7
ACCESSION NUMBER: 93389199 MEDLINE
DOCUMENT NUMBER: 93389199 PubMed ID: 8376802
TITLE: Antigen-reactive gamma delta T cells in human **leishmaniasis**.
AUTHOR: Russo D M; Armitage R J; Barral-Netto M; Barral A;

Grabstein K H; Reed S G
CORPORATE SOURCE: Seattle Biomedical Research Institute, Washington 98109.
CONTRACT NUMBER: AI08392 (NIAID)
AI16282 (NIAID)
AI25038 (NIAID)
SOURCE: JOURNAL OF IMMUNOLOGY, (1993 Oct 1) 151 (7) 3712-8.
Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journa
ENTRY MONTH: 199310
ENTRY DATE: Entered STN: 19931105
Last Updated on STN: 19931105
Entered Medline: 19931021

AB The importance of Ag-specific gamma delta T lymphocytes in huma immune responses to pathogenic organisms is unknown. In the pr study the expression of gamma delta TCR on T lymphocytes from patients with cutaneous, mucosal, or visceral **leishmaniasis** was examined. All of these patient groups had elevated levels gamma delta T cells in peripheral blood. Patients' gamma delta cells included CD8+ as well as null cells. The percentage of T cells expressing gamma delta TCR was increased significantly by stimulation in vitro with certain parasite Ag. T-cell lines generated by stimulation with promastigote **lysates** of **Leishmania amazonensis** or **L. braziliensis** typically contained 25 to 60% gamma delta T cells. In contrast, two immunodominant surface Ag of **L. amazonensis**, gp63 and gp42, did not expand gamma delta T cells from infected patients, although both Ag elicited strong alpha beta T-cell responses. gamma delta T cells isolated from a **Leishmania**-specific T-cell line responded to stimulation with promastigote **lysate**. Of particular interest, gamma delta T cells from PBMC of a patient with mucosal **leishmaniasis** responded to stimulation with a recombinant 70 kDa **heat** shock protein of **L. chagasi**. This study demonstrated that several clinical forms of **leishmaniasis** induced elevated numbers of gamma delta T cells that responded specifically to **Leishmania** Ag in vitro. Therefore, this component of the T-cell response to **Leishmania** may impact the outcome of clinical disease.

L30 ANSWER 15 OF 19 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1993:455350 BIOSIS
DOCUMENT NUMBER: PREV199396100250
TITLE: Proteinase activity in the isolates of Trichomonas vaginalis according to their pathogenicity.
AUTHOR(S): Shim, Young-Ki; Park, Kyung-Hee; Chung, Pyung-Rim; Im, Kyung-Il (1)
CORPORATE SOURCE: (1) Dep. Parasitology, Coll. Med., Inst. Tropical Med., Yonsei Univ., Seoul 120-752 North Korea
SOURCE: Korean Journal of Parasitology, (1993) Vol. 31, No. 2, pp. 117-127.
ISSN: 0368-6809.
DOCUMENT TYPE: Article
LANGUAGE: Korean
SUMMARY LANGUAGE: Korean; English

AB Ten axenic isolates of Trichomonas vaginalis were subcutaneously injected to the BALB/c mice in order to assess their pathogenicity by means of so-called 'mouse assay' method. All the isolates revealed neutral and acid proteinase activities both in their **lysates** and in culture media, but the specific activities of both proteinases in the severely pathogenic group were significantly higher than the mildly pathogenic group (p lt 0.05). In the SDS-PAGE system in which the electrophoretic gels contained 0.4% gelatin as the substrate, five different banding patterns of trichomonal proteinases were detected, and the patterns were closely related with the pathogenicity of the isolates of T. vaginalis. All five bands might be regarded as cysteine proteinases group in the inhibitor assays. The cytotoxicity of the **lysates** of T vaginalis to the target Chinese hamster ovarian (CHO) cell line was also significantly different according to the pathogenicity of the isolates, and generally lower in the **lysates** treated with cysteine proteinase inhibitors than in the control **lysates** . In summarizing the results, it might be considered that the proteinases of T. vaginalis showing five electrophoretic banding patterns are closely related with the pathogenicity and cytotoxicity of the isolates of T. vaginalis.

L30 ANSWER 16 OF 19 MEDLINE DUPLICATE 8
ACCESSION NUMBER: 93301586 MEDLINE
DOCUMENT NUMBER: 93301586 PubMed ID: 7686209
TITLE: **Leishmania major**-specific, CD4+, major histocompatibility complex class II-restricted T cells derived in vitro from lymphoid tissues of naive mice.
AUTHOR: Shankar A H; Titus R G
CORPORATE SOURCE: Department of Tropical Public Health, Harvard School of Public Health, Boston, Massachusetts 02115.
CONTRACT NUMBER: AI-29955 (NIAID)
SOURCE: JOURNAL OF EXPERIMENTAL MEDICINE, (1993 Jul 1) 178 (1) 101-11.
Journal code: 2985109R. ISSN: 0022-1007.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199307
ENTRY DATE: Entered STN: 19930813
Last Updated on STN: 19960129
Entered Medline: 19930723

AB Several studies indicate that the outcome of experimental murine cutaneous **leishmaniasis** caused by **Leishmania major** (Lm) is determined by immunological events occurring shortly after infection. These events lead to outgrowth of either protective CD4+ T cells in the C57BL/6 mouse, which cures, or exacerbative cells in the BALB/c mouse, which succumbs to disease. Potential factors influencing the outgrowth of protective or exacerbative T cells include antigen-presenting cells (APC), cytokines, and parasite antigens. An in vitro system, in which one could precisely control the factors shaping early events in the T cell response to Lm, would be very useful. To this end, we have examined the in vitro response of naive lymphocytes to Lm promastigotes. The data presented here show that Lm-specific CD4+ T cell receptor alpha/beta + T cells can be generated in vitro from

spleen and lymph node cell populations of naive mice. Furthermore, they can be obtained from the CD44low (unprimed) population of T lymphocytes, indicating that in vitro priming occurs. The ability to generate these T cells is dependent on the presence of live parasites and is not due to a parasite-derived nonspecific T cell mitogen. Restimulation, as assayed by proliferation, requires APC bearing syngeneic I-A. Optimal restimulation of the in vitro derived T cells is achieved only when live promastigotes are used. The T cells do not proliferate in response to a frozen-and-thawed **lysate** of promastigotes, yet they exhibit mild reactivity to **lysates** prepared from **heat**-shocked promastigotes. Furthermore, they do not recognize two predominant antigens on the promastigote surface, lipophosphoglycan and gp63. T cells derived in vitro with Lm show crossreactivity with live **L. donovani**, less crossreactivity with live **L. mexicana**, and no crossreactivity with live Bacillus-Calmette-Guerin or live Brugia malayi microfilariae. Finally, these early T cells, whether derived from healing C57BL/6 or nonhealing BALB/c mice, produce interleukin 2 (IL-2), IL-4, and interferon gamma.

L30 ANSWER 17 OF 19 MEDLINE DUPLICATE 9
ACCESSION NUMBER: 92006650 MEDLINE
DOCUMENT NUMBER: 92006650 PubMed ID: 1833139
TITLE: Analysis of primary T cell responses to intact and fractionated microbial pathogens.
AUTHOR: Pfeffer K; Schoel B; Gulle H; Moll H; Kromer S; Kaufmann S H; Wagner H
CORPORATE SOURCE: Institute of Medical Microbiology and Hygiene, Technical University of Munich, FRG.
SOURCE: CURRENT TOPICS IN MICROBIOLOGY AND IMMUNOLOGY, (1991) 173 173-8.
Journal code: 0110513. ISSN: 0070-217X.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199111
ENTRY DATE: Entered STN: 19920124
Last Updated on STN: 19920124
Entered Medline: 19911107

AB Freshly isolated human T lymphocytes were tested for their response to mycobacteria, mycobacterial **lysates**, 2 dimensional (2D) PAGE separated mycobacterial **lysates**, **leishmania** and defined **leishmanial** antigen preparations. While gamma delta T cells proliferated vigorously in the presence of mycobacteria and mycobacteria derived **lysates**, a significant stimulation from 2 D gel separated **lysates** was not detected. In addition gamma delta T cells failed to respond towards **leishmania** or **leishmanial** components. In the alpha beta T cell compartment some donors, presumably according to their state of immunity against mycobacteria, responded to mycobacteria, mycobacterial **lysates** and 2 D gel separated mycobacterial **lysates**. Neither freshly isolated gamma delta T cells nor alpha beta T cells from naive donors did mount a significant immune response against **leishmania**.

L30 ANSWER 18 OF 19 SCISEARCH COPYRIGHT 2003 THOMSON ISI

ACCESSION NUMBER: 91:446404 SCISEARCH
THE GENUINE ARTICLE: GA068
TITLE: ANALYSIS OF PRIMARY T-CELL RESPONSES TO INTACT AND FRACTIONATED MICROBIAL PATHOGENS
AUTHOR: PFEFFER K (Reprint); SCHOEL B; GULLE H; MOLL H; KROMER S; KAUFMANN S H E; WAGNER H
CORPORATE SOURCE: TECH UNIV MUNICH, INST MED MICROBIOL & HYG, W-8000 MUNICH 2, GERMANY (Reprint); UNIV ERLANGEN NURNBERG, INST CLIN MICROBIOL, W-8520 ERLANGEN, GERMANY; UNIV ULM, INST MED MICROBIOL, W-7900 ULM, GERMANY
COUNTRY OF AUTHOR: GERMANY
SOURCE: CURRENT TOPICS IN MICROBIOLOGY AND IMMUNOLOGY, (1991) Vol. 173, pp. 173-178.
DOCUMENT TYPE: Article; Journal
LANGUAGE: ENGLISH
REFERENCE COUNT: 18

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Freshly isolated human T lymphocytes were tested for their response to mycobacteria, mycobacterial **lysates**, 2 dimensional (2D) PAGE separated mycobacterial **lysates**, **leishmania** and defined **leishmanial** antigen preparations. While gamma-delta-T cells proliferated vigourously in the presence of mycobacteria and mycobacteria derived **lysates**, a significant stimulation from 2 D gel separated **lysates** was not detected. In addition gamma-delta-T cells failed to respond towards **leishmania** or **leishmanial** components. In the alpha-beta-T cell compartment some donors, presumably according to their state of immunity against mycobacteria, responded to mycobacteria, mycobacterial **lysates** and 2 D gel separated mycobacterial **lysates**. Neither freshly isolated gamma-delta-T cells nor alpha-beta-T cells from naive donors did mount a significant immune response against **leishmania**.

L30 ANSWER 19 OF 19 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1982:223386 BIOSIS
DOCUMENT NUMBER: BA73:83370
TITLE: **LEISHMANIA-TROPICA** ASSOCIATION OF A B CELL MITOGEN WITH HYPER GAMMA GLOBULINEMIA IN MICE.
AUTHOR(S): WEINTRAUB J; GOTTLIEB M; WEINBAUM F I
CORPORATE SOURCE: WHO IMMUNOLOGY RESEARCH AND TRAINING CENTRE, HOPITAL CANTONAL UNIVERSITAIRE DE GENEVA, 1211 GENEVA 4, SWITZERLAND.
SOURCE: EXP PARASITOL, (1982) 53 (1), 87-96. CODEN: EXPAAA. ISSN: 0014-4894.
FILE SEGMENT: BA; OLD
LANGUAGE: English

AB Infection of BALB/c mice with **L. tropica** NIH S strain resulted in splenic enlargement, hypergammaglobulinemia, and polyclonal activation of B lymphocytes as measured by the splenic plaque-forming cell response (PFC) to trinitrophenyl (TNP) and sheep erythrocytes (SRBC). The peak anti-SRBC PFC response occurred 5 wk after infection; both direct and indirect (facilitated) plaques were significantly increased. The in vitro primary immune response to trinitrophenyl haptenated lipopolysaccharide (TNP-LPS), as enumerated by the anti-TNP PFC response, was increased on a per spleen basis beginning 3 wk after infection. The properties of a

lysate of **L. tropica** promastigotes (LTL) was studied to determine whether polyclonal B-cell activation was related to a parasite-derived mitogen. A B-cell mitogen was identified in LTL which stimulated the proliferation of spleen cells in vitro from uninfected control and congenitally athymic (T-cell-deficient) but not from .mu.-suppressed (B-cell-deficient) animals. Preliminary characterization of the mitogen material indicated that it was a nonpyrogenic, **heat**-labile peptide or protein and was probably not bacterial lipopolysaccharide (LPS).

FILE 'REGISTRY' ENTERED AT 11:46:59 ON 08 MAY 2003
E HYDROCORTISONE/CN
L31 4 S (EPINEPHRINE OR DIPHENHYDRAMINE OR METHYL PREDNISOLONE
E METHYL PREDNISOLONE/CN 5

FILE 'HCAPLUS' ENTERED AT 11:48:26 ON 08 MAY 2003
L22 7054 SEA FILE=HCAPLUS ABB=ON PLU=ON LEISHMAN? OR (LEISHMAN? OR L)(W)(TROPICA OR MEXICAN? OR GUYANEN? OR BRAZIL? OR MAJOR OR DONOVAN? OR CHAGASI OR AMAZONEN? OR PERUVIAN? OR PANAMEN? OR PIFANOI OR INFANTUM OR AETHIOPIC?)
L31 4 SEA FILE=REGISTRY ABB=ON PLU=ON (EPINEPHRINE OR DIPHENHYDRAMINE OR METHYL PREDNISOLONE OR HYDROCORTISONE OR ACETAMINOPHEN OR DIPHENHYDRAMINE)/CN
L32 91132 SEA FILE=HCAPLUS ABB=ON PLU=ON L31 OR EPINEPHRINE OR DIPHENHYDRAMINE OR DI PHENHYDRAMINE OR DIPHEN HYDRAMINE OR (ME OR METHYL)(W)PREDNISOLONE OR HYDROCORTISONE OR HYDRO CORTISONE OR ACETAMINOPHEN
L33 15 SEA FILE=HCAPLUS ABB=ON PLU=ON L22 AND L32

L34 14 L33 NOT L26

L34 ANSWER 1 OF 14 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2003:42386 HCAPLUS
DOCUMENT NUMBER: 138:86119
TITLE: Novel human hepatoma lines, methods for obtaining same and uses thereof
INVENTOR(S): Gripon, Philippe; Rumin, Sylvie; Guguen-Guillouzo, Christiane; Trepo, Christian
PATENT ASSIGNEE(S): Institut National De La Sante Et De La Recherche Medicale (I.N.S.E.R.M.), Fr.
SOURCE: PCT Int. Appl., 74 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003004627	A2	20030116	WO 2002-FR2391	20020708

W: CA, JP, US
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR
PRIORITY APPLN. INFO.: FR 2001-9044 A 20010706
AB The invention concerns human hepatoma cell lines, characterized in that they are capable of being naturally infected by parasites and/or viruses; said parasites can be hepatotropic or not, such as Plasmodium or parasites of the genus **leishmania** and

express receptors of the family of Flaviviridae and Hepadnaviridae viruses, preferably HBV and HCV. The invention has diagnostic, therapeutic and prophylactic applications.

L34 ANSWER 2 OF 14 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:539482 HCAPLUS
DOCUMENT NUMBER: 137:99011
TITLE: Film-forming polymers for topical compositions for treatment of nails and skin
INVENTOR(S): Dvoretzky, Israel; Kuleza, John E.
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002055023	A2	20020718	WO 2002-US282	20020107
WO 2002055023	A3	20021107		

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-260430P P 20010109

AB An easily employed, convenient, consumer-oriented treatment system for nails and/or skin surfaces for a wide variety of medical problems is achieved by providing a film forming compn. incorporating one or more therapeutic substances which can be employed independently or, if desired, in combination with an easily employed holding or support member for delivering heat directly to the application site. In particular, diseases, disorders, and medical conditions of nails and/or skin include, but are not limited to, psoriasis, skin cancers, warts, **leishmaniasis**, mycobacteria, and granuloma annulare. For example, a preferred formulation contains clobetasol propionate 0.05%, urea 3%, di-Bu phthalate 1.5%, Eudragit RL 100 7%, ethanol 70%, and water up to 100%.

IT **50-23-7, Hydrocortisone 58-73-1, Diphenhydramine**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (topical compns. contg. film-forming polymers for treatment of disorders of nails and skin)

L34 ANSWER 3 OF 14 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:642258 HCAPLUS
DOCUMENT NUMBER: 133:293391
TITLE: Inhibitory and lytic effects of phenothiazine derivatives and related tricyclic neuroleptic compounds, on Entamoeba histolytica HK9 and HMI

trophozoites

AUTHOR(S): Ondarza, Raul N.; Hernandez, Eva; Iturbe, Angelica; Hurtado, Gerardo

CORPORATE SOURCE: Center of Research on Infectious Diseases, National Institute of Public Health, Mexico, 62508, Mex.

SOURCE: Biotechnology and Applied Biochemistry (2000), 32(1), 61-67
CODEN: BABIEC; ISSN: 0885-4513

PUBLISHER: Portland Press Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB It has been shown previously that tricyclic neuroleptics like clomipramine and chlorpromazine have lethal effects on **Leishmania donovani** and **L. major**, and other studies indicate that the phenothiazine inhibitors of trypanothione reductase are potential anti-trypanosomal and anti-**leishmanial** drugs. With this in mind, the authors examd. the possible inhibitory effects of various phenothiazine and tricyclic derivs. on Entamoeba histolytica. It was found that drugs like clomipramine (KD002), the most potent in vitro inhibitor of trypanothione reductase among 30 tricyclic compds. tested, at 25 .mu.M after 24 h of culture under aerobic conditions, caused a substantial decrease in the no. of E. histolytica HK9 trophozoites, from approx. 15 .times. 106 to 5.37 .times. 106 cells, and at 100 .mu.M to 0.8 .times. 106 cells. A substantial inhibitory effect on cell proliferation could also be demonstrated with metronidazol (used clin. against amoebiasis). Under similar exptl. conditions, other tricyclic and phenothiazine derivs. (OFKs), designed originally to inhibit the trypanothione reductase of trypanosomatides, had an inhibitory effect of 16 to 95%. For comparison, similar results were obtained using clomipramine and a phenothiazine deriv. (OFK006) with Trypanosoma cruzi and Crithidia luciliae, except that with the latter the inhibitory effect of clomipramine was less dramatic. Expts. comparing two E. histolytica strains showed that normal cell proliferation under anaerobiosis was higher in strain HK9 than in HM1, which is highly virulent, but that metronidazol and clomipramine were less effective against HM1. Two other drugs tested, diphenydramine (KD005) and a phenothiazine deriv. (OFK008), also had significant but lower inhibitory effects on both strains. The inhibitory activity on cell proliferation and the lytic effects on this human parasite by the tricyclic compds. clomipramine, chlorpromazine and others, as well as by the phenothiazine derivs., indicate that they can be considered potential anti-amoebic agents.

IT **58-73-1, Diphenhydramine**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitory and lytic effects of phenothiazine derivs. and related tricyclic neuroleptic compds. on Entamoeba histolytica trophozoites)

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 4 OF 14 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:82762 HCAPLUS
DOCUMENT NUMBER: 132:217287

TITLE: Effects of immunosuppressive therapy on murine **Leishmania infantum** visceral **leishmaniosis**
AUTHOR(S): Gangneux, Jean-Pierre; Chau, Francoise; Sulahian, Annie; Derouin, Francis; Garin, Yves Jean-Francois
CORPORATE SOURCE: Laboratoire de Parasitologie-Mycologie, Faculte de Medecine Lariboisiere Saint-Louis, Paris, 75270, Fr.
SOURCE: European Cytokine Network (1999), 10(4), 557-559
CODEN: ECYNEJ; ISSN: 1148-5493
PUBLISHER: John Libbey Eurotext
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We evaluated the effect of immunosuppressive therapy on the course of infection, the spleen cell immunophenotype and cytokine prodn. during murine **Leishmania infantum** visceral **leishmaniosis** (VL). Rousseau et al. [1] recently reported that prolonged administration of dexamethasone induces limited reactivation of chronic murine visceral **leishmaniosis**, with no clear Th1-Th2 cytokine patterns. We found that another glucocorticoid, **hydrocortisone** acetate, had similar effects during acute visceral **leishmaniosis**, i.e. an increase in parasite burden in the spleen, but not the liver, of infected mice. A significant increase in parasite burden in both the liver and the spleen was only achieved when mice were treated with combined dexamethasone + pentoxifylline immunotherapy; increases in parasite burden were never assocd. with a specific spleen cell immunophenotype or a Th1-Th2 cytokine secretion profile.

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 5 OF 14 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:520418 HCAPLUS
DOCUMENT NUMBER: 131:165010
TITLE: Amphotericin B deoxycholate treatment of visceral **leishmaniasis** with newer modes of administration and precautions: a study of 938 cases
AUTHOR(S): Thakur, C. P.; Singh, R. K.; Hassan, S. M.; Kumar, R.; Narain, S.; Kumar, Ashok
CORPORATE SOURCE: Balaji Utthan Sansthan, Patna, 800 001, India
SOURCE: Transactions of the Royal Society of Tropical Medicine and Hygiene (1999), 93(3), 319-323
CODEN: TRSTAZ; ISSN: 0035-9203
PUBLISHER: Royal Society of Tropical Medicine and Hygiene
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Out of 938 parasitol. confirmed patients with visceral **leishmaniasis** treated with amphotericin B (1 mg/kg bodyweight daily infused in 2 h for 20 days), 935 were cured clin., 933 parasitol. and 931 ultimately (no relapse within 6 mo). Two parasitol. 'not cured' and 4 relapsed patients were cured with 25 infusions, and 1 with double relapse with 30 infusions. The treatment was started only when serum Hb reached 5 g/dL, serum electrolyte imbalance was cor. and sodium stibogluconate-induced myocardial damage stabilized after 10 days' rest. Bronchopneumonia,

cardiac failure and acute renal failure caused the death of 1 patient each. Nightblindness, angular stomatitis, neuritis, and petechial hemorrhages improved with appropriate treatment; 2 patients were given blood transfusion for post-treatment anemia. Nausea and anorexia, and changes in serum creatinine and potassium, became normal in 2 wk. Immediate withdrawal of the drug and restart after 10 days cured 2 patients who developed acute renal failure. Infusion-related toxicities-shivering, rigor and fever-were minimized but not eliminated by prior administration of **hydrocortisone**. Tuberculosis and visceral **leishmaniasis** were treated concurrently. Four pregnant patients were successfully treated without harmful effects on mother and child. It was concluded that the dosage of amphotericin B used was an effective and well-tolerated regimen and achieved 99% cure. Toxicity could be minimized with some precautions. All unresponsive and relapsed patients responded to more amphotericin and no resistance to the drug was seen.

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 6 OF 14 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:527193 HCAPLUS
DOCUMENT NUMBER: 129:166193
TITLE: Therapeutic treatment and prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix
INVENTOR(S): Setterstrom, Jean A.; Van Hamont, John E.; Reid, Robert H.; Jacob, Elliot; Jeyanthi, Ramasubbu; Boedeker, Edgar C.; McQueen, Charles E.; Tice, Thomas R.; Roberts, F. Donald; Friden, Phil
PATENT ASSIGNEE(S): United States Dept. of the Army, USA; Van Hamont, John E.; et al.
SOURCE: PCT Int. Appl., 363 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 13
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9832427	A1	19980730	WO 1998-US1556	19980127
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 6309669	B1	20011030	US 1997-789734	19970127
AU 9863175	A1	19980818	AU 1998-63175	19980127

PRIORITY APPLN. INFO.:
US 1997-789734 A 19970127
US 1984-590308 B1 19840316
US 1992-867301 A2 19920410

US 1995-446148	A2	19950522
US 1995-446149	B2	19950522
US 1996-590973	B2	19960124
WO 1998-US1556	W	19980127

AB Novel burst-free, sustained release biocompatible and biodegradable microcapsules are disclosed which can be programmed to release their active core for variable durations ranging from 1-100 days in an aq. physiol. environment. The microcapsules are comprised of a core of polypeptide or other biol. active agent encapsulated in a matrix of poly(lactide/glycolide) copolymer, which may contain a pharmaceutically acceptable adjuvant, as a blend of upcapped free carboxyl end group and end-capped forms ranging in ratios from 100/0 to 1/99.

IT **50-23-7, Hydrocortisone 58-73-1, Diphenhydramine 103-90-2, Acetaminophen**
RL: BPR (Biological process); BSU (Biological study, unclassified); DEV (Device component use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(prevention of infections with bioactive material encapsulated within biodegradable-biocompatible polymeric matrix)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 7 OF 14 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:471443 HCAPLUS
DOCUMENT NUMBER: 129:105238
TITLE: Method of transcriptionally modulating gene expression and of discovering chemicals capable of functioning as gene expression modulators
INVENTOR(S): Foulkes, J. Gordon; Franco, Robert; Leichtfried, Franz; Pieler, Christian; Stephenson, John R.
PATENT ASSIGNEE(S): Oncogene Science, Inc., USA
SOURCE: U.S., 64 pp., Division of U. S. Ser. No. 306,925.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5776502	A	19980707	US 1995-458691	19950602
PRIORITY APPLN. INFO.:			US 1989-382711	19890718
			US 1993-26270	19930304
			US 1994-306925	19940915

AB A method of modulating transcription of a gene assocd. with a defined physiol. or pathol. effect in a multicellular organism comprises contacting the cell with a substance which does not normally occur in the cell, which specifically modulates transcription of the gene, and which binds to DNA or RNA, or to a protein at a site other than a normal ligand-binding domain. A method of identifying such transcription-modulating substances comprises contacting a cell sample with the substance, said cells contg. a modulatable transcriptional regulatory sequence and a promoter of the gene of interest fused to a reporter gene. Plasmids contg. the luciferase gene fused to mouse mammary tumor virus

promoter, human granulocyte colony-stimulating factor promoter, or human growth hormone promoter were prepd., and cell lines contg. these constructs were produced. These transformants were used for high-throughput screening of 2000 chems.

IT **50-23-7, Hydrocortisone**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(method of transcriptionally modulating gene expression and of discovering chems. capable of functioning as gene expression modulators)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 8 OF 14 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:25141 HCAPLUS
DOCUMENT NUMBER: 128:84748
TITLE: Compositions and methods for the treatment of chronic infection
INVENTOR(S): Rook, Graham Arthur William; Pando, Hernandez Rogelio
PATENT ASSIGNEE(S): Stanford Rook Ltd., UK; Rook, Graham Arthur William; Pando Hernandez, Rogelio;
SOURCE: PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9748367	A2	19971224	WO 1997-GB1653	19970618
WO 9748367	A3	19980205		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9731030	A1	19980107	AU 1997-31030	19970618

PRIORITY APPLN. INFO.: GB 1996-12990 19960620
WO 1997-GB1653 19970618

AB A glucocorticoid, such as cortisol or a deriv. or analog thereof, and an anti-glucocorticoid, such as dehydroepiandrosterone (DHEA) or a deriv. or analog thereof, are used simultaneously, sep. or sequentially in treatment of chronic infections such as tuberculosis, HIV infection, **leishmaniasis** and syphilis.

IT **50-23-7**, Cortisol
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. and methods for treatment of chronic infection with glucocorticoids and antiglucocorticoids)

L34 ANSWER 9 OF 14 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1995:998462 HCAPLUS
DOCUMENT NUMBER: 124:25449
TITLE: Cyclic AMP mediates change in superoxide dismutase activity to monitor host-parasite interaction in **Leishmania donovani**
AUTHOR(S): Dey, Runu; Mitra, Smita; Datta, Salil C.
CORPORATE SOURCE: Indian Institute of Chemical Biology, Calcutta, 700032, India
SOURCE: Journal of Parasitology (1995), 81(5), 683-6
CODEN: JOPAA2; ISSN: 0022-3395
PUBLISHER: American Society of Parasitologists
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The present study is designed to understand the role of cAMP in host-parasite interaction involving **Leishmania donovani**, the causative agent for Kala-azar. When **Leishmania** promastigotes or macrophages were pretreated with dibutyryl cAMP or theophylline and **epinephrine**, which are well-defined initiators for cAMP release, a key enzyme of the oxygen defense system, superoxide dismutase (SOD), was inhibited. At the same time, parasite interaction was considerably reduced to the level of 54.5% and 46.2%, resp., for pretreated promastigotes. Internalization of the organisms in phagolysosomes was similarly affected. Dibutyryl cAMP-treated promastigotes in the presence of SOD, on the other hand, restored in vitro infection to the normal level. At least 50% less cAMP entered into **Leishmania** promastigotes when SOD was added to the incubation system contg. dibutyryl cAMP. Data reveal that cAMP perturbs the **Leishmania**-macrophage interaction through inhibition of SOD, pointing to the importance of a promastigote enzyme for the survival of this pathogen within phagolysosomes.

L34 ANSWER 10 OF 14 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1995:760517 HCAPLUS
DOCUMENT NUMBER: 123:141460
TITLE: Effect of PGE2 and of agents that raise cAMP levels on macrophage activation induced by IFN-.gamma. and TNF-.alpha.
AUTHOR(S): Mauel, Jacques; Ransiijn, Adriana; Corradin, Sally Betz; Buchmuller-Rouiller, Yolande
CORPORATE SOURCE: Institute of Biochemistry, Epalinges, Switz.
SOURCE: Journal of Leukocyte Biology (1995), 58(2), 217-24
CODEN: JLBIE7; ISSN: 0741-5400
PUBLISHER: Federation of American Societies for Experimental Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The effect of prostaglandin (PGE2) on macrophage activation by interferon-.gamma. (IFN-.gamma.) and tumor necrosis factor-.alpha. (TNF-.alpha.) was evaluated. Murine macrophages infected with **Leishmania** enriettii or **Leishmania major** were activated by exposure to IFN-.gamma. (10-50 U/ml) and TNF-.alpha. (30-3000 U/ml), leading to intracellular parasite destruction within 24-48 h. **Leishmanicidal** activity was markedly increased when activation was performed in the presence of

PGE2 (10-9-10-7 M) or arachidonate (10-5 M, a PG precursor), concomitant with enhanced nitrite release and glucose oxidn. through the hexose monophosphate shunt pathway. Conversely, activation was reduced by indomethacin and **hydrocortisone**, two inhibitors of PG synthesis. Parasite killing and nitrite prodn. were fully restored by exogenous PGE2, indicating that inhibition by these drugs was related to their ability to block PG prodn. PG can stimulate adenylate cyclase, thus raising intracellular cAMP levels. Accordingly, dibutyryl-cAMP, theophylline (which prevents cAMP breakdown), and forskolin (an activator of adenylate cyclase) all stimulated macrophage activation. Finally, PGE2 and cAMP enhanced expression of inducible nitric oxide synthase mRNA in response to IFN-.gamma. and TNF-.alpha., and this effect was inhibited by the cAMP antagonist 2'-O-Me adenosine. These findings are consistent with the hypothesis that PGE2 acts as a pos. agonist in macrophage activation by IFN-.gamma. and TNF-.alpha. via its capacity to modulate intracellular cAMP levels.

L34 ANSWER 11 OF 14 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1992:424053 HCAPLUS
DOCUMENT NUMBER: 117:24053
TITLE: Effect of bioamines on uptake of promastigotes of **Leishmania donovani** by hamster peritoneal macrophages
AUTHOR(S): Mitra, Smita; Ghosh, Lagnajita; Chakrabarty, Pampa; Biswas, Madhumita; Bhattacharyya, F. Kethlene; Ghosh, D. K.
CORPORATE SOURCE: Dep. Immunochem., Indian Inst. Chem. Biol., Calcutta, 700 032, India
SOURCE: Journal of Medical Microbiology (1992), 36(4), 283-7
CODEN: JMMIAV; ISSN: 0022-2615
DOCUMENT TYPE: Journal
LANGUAGE: English
AB **Epinephrine** and norepinephrine inhibit attachment of **L. donovani** promastigotes to cultured hamster peritoneal macrophages. The inhibition was significant at catecholamine concns. of 10-4 and 10-5M and occurred when they were added to the cell mixts., or after pre-treatment of either macrophages or parasites. Inhibition of attachment after pretreatment was less marked than when the catecholamines were added to parasite-cell mixts. Similar results were obtained with dibutyryl cAMP, cholera toxin, theophylline, and cadaverine which raise intracellular cAMP. Pretreatment of parasites or macrophages with the bioamines elevated the intracellular cAMP concn. It is suggested that the inhibitory effect on the host-parasite interaction is mediated through cAMP.
IT **51-43-4, Epinephrine**
RL: BIOL (Biological study)
(**Leishmania donovani** promastigotes attachment to peritoneal macrophages inhibition by)

L34 ANSWER 12 OF 14 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1990:30776 HCAPLUS
DOCUMENT NUMBER: 112:30776
TITLE: Effect of **hydrocortisone** acetate on the white cell series of bone marrow of albino rats

AUTHOR(S): Naresh, Manju; Chandra, Naresh; Sakhuja, Suman; Chanda, Avinash
CORPORATE SOURCE: Dep. Anat., B. R. D. Med. Coll., Gorakhpur, India
SOURCE: Indian Journal of Physiology and Allied Sciences (1989), 43(3), 97-104
CODEN: IJPLAN; ISSN: 0367-8350
DOCUMENT TYPE: Journal
LANGUAGE: English

AB To det. the effect on the bone marrow of albino rats, 0.6 mg **hydrocortisone** acetate dissolved in 0.4 mL of propylene glycol was given by i.m. route, daily. Control and treated rats were sacrificed at weekly intervals for 12 wk. Bone marrow was taken from the shafts of femora, smears were made with a uniform cell suspension obtained by mixing the bone marrow with N/10 normal saline, and they were stained with **Leishman**'s stain. The granular cells of white cell series show myeloid stimulation reflected mainly on neutrophils and more marked in female than in male treated rats. In addn., there is a decrease in eosinophils and basophils count. No significant change was noticed in myeloblasts, promyelocytes, myelocytes, and metamyelocytes in the rats of both the sexes. In nongranular cells of white cell series the lymphocytes show a decrease. No significant change is noticed in monocytes, plasma cells, and megakaryocytes. The myeloid-erythroid ratio shows a slight decrease in treated rats of both sexes.

IT **50-23-7, Hydrocortisone**
RL: BIOL (Biological study)
(bone marrow white cell series response to)

L34 ANSWER 13 OF 14 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1989:205119 HCAPLUS
DOCUMENT NUMBER: 110:205119
TITLE: In vitro anti-**leishmanial** activity of compounds in current clinical use for unrelated diseases
AUTHOR(S): Neal, R. A.; Allen, S.
CORPORATE SOURCE: Dep. Med. Protozool., London Sch. Hyg. Trop. Med., St. Albans/Herts., UK
SOURCE: Drugs under Experimental and Clinical Research (1988), 14(10), 621-8
CODEN: DECRDP; ISSN: 0378-6501
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Drugs in current clin. use were tested for anti-**Leishmania** activity using an in vitro infected macrophage assay. Out of almost 400 compds. tested, over 100 were active. The most active compds. showed ED50 values below 1 .mu.M. The active compds. should be tested in in vivo systems. They made lead to the development of new antileishmanials.

IT **58-73-1**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**Leishmania donovani** inhibition by)

L34 ANSWER 14 OF 14 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1959:84749 HCAPLUS
DOCUMENT NUMBER: 53:84749

ORIGINAL REFERENCE NO.: 53:15303i,15304a
TITLE: Inhibition of intracutaneous **leishmanin** reaction by **hydrocortisone** acetate
AUTHOR(S): Dostrovsky, A.; Cohen, H. A.
CORPORATE SOURCE: Hebrew Univ., Jerusalem
SOURCE: J. Invest. Dermatol. (1957), 29, 15-26
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

AB The reaction to subcutaneous injection of **leishmanin** antigen was slightly suppressed by systemic administration of cortisone and adrenocorticotropic hormone, but was completely suppressed by injection of 2.5 mg. **hydrocortisone** acetate together with the antigen. The reaction was not affected by intracutaneous cortisone, adrenocorticotropic hormone, or hyaluronidase with the vaccine. A fully developed **leishmanin** test was suppressed by intracutaneous injection of **hydrocortisone**. Histologically the degree of infiltration at the suppressed test site was diminished.

(FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO' ENTERED AT 11:50:36 ON 08 MAY 2003)

L35 66 S L33
L36 66 S L35 NOT L29
L37 45 DUP REM L36 (21 DUPLICATES REMOVED)
L38 5 S L37 AND ANTIBOD?
L39 15 S L37 AND (VACCIN? OR IMMUN?)
L40 18 S L38 OR L39

L40 ANSWER 1 OF 18 MEDLINE
ACCESSION NUMBER: 2000053994 MEDLINE
DOCUMENT NUMBER: 20053994 PubMed ID: 10586123
TITLE: Effects of **immunosuppressive** therapy on murine **Leishmania infantum** visceral **leishmaniosis**.
COMMENT: Comment on: Eur Cytokine Netw. 1998 Dec;9(4):655-61
AUTHOR: Gangneux J P; Chau F; Sulahian A; Derouin F; Garin Y J
CORPORATE SOURCE: Laboratoire de Parasitologie-Mycologie, Faculte de Medecine Lariboisiere-Saint-Louis, 15, rue de l'Ecole-de-Medecine, 75270 Paris Cedex 06, France.
SOURCE: EUROPEAN CYTOKINE NETWORK, (1999 Dec) 10 (4) 557-9. Journal code: 9100879. ISSN: 1148-5493.
PUB. COUNTRY: France
DOCUMENT TYPE: Commentary
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 200002
ENTRY DATE: Entered STN: 20000218
Last Updated on STN: 20000512
Entered Medline: 20000210

AB We evaluated the effect of **immunosuppressive** therapy on the course of infection, the spleen cell **immunophenotype** and cytokine production during murine **Leishmania infantum** visceral **leishmaniosis** (VL). Rousseau et al. [1] recently reported that prolonged administration of dexamethasone induces limited reactivation of chronic murine visceral **leishmaniosis**, with no clear Th1-Th2 cytokine

patterns. We found that another glucocorticoid, **hydrocortisone** acetate, had similar effects during acute visceral **leishmaniosis**, i.e. an increase in parasite burden in the spleen, but not the liver, of infected mice. A significant increase in parasite burden in both the liver and the spleen was only achieved when mice were treated with combined dexamethasone + pentoxifylline **immunotherapy**; increases in parasite burden were never associated with a specific spleen cell **immunophenotype** or a Th1-Th2 cytokine secretion profile.

L40 ANSWER 2 OF 18 MEDLINE
ACCESSION NUMBER: 95116199 MEDLINE
DOCUMENT NUMBER: 95116199 PubMed ID: 7816511
TITLE: [The host-opportunistic protozoa system. The dissemination of **Leishmania infantum** infection in naturally susceptible laboratory animals subjected to drug-induced **immunosuppression**].
Sistema "khoziain--uslovno-patogennye prosteishie". Disseminatsiia infektsii **Leishmania infantum** u estestvenno vospriimchivykh laboratornykh zhivotnykh, podvergnutykh medikamentoznoi **immunosupressii**.
AUTHOR: Kovalenko F P; Lysenko A Ia; Lavdovskaia M V
SOURCE: PARAZITOLOGIIA, (1994 Jul-Aug) 28 (4) 293-7.
Journal code: 0101672. ISSN: 0031-1847.
PUB. COUNTRY: RUSSIA: Russian Federation
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Russian
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199502
ENTRY DATE: Entered STN: 19950217
Last Updated on STN: 19950217
Entered Medline: 19950209

AB The possibility to awake the disseminated infection of **Leishmania infantum** in golden hamsters Mesocricetus auratus, hispid cotton rats Sigmodon hispidus, soft furred rats Mastomys natalensis by means of different **immunodepressants** has been examined. On the background of the **immunosuppression** caused by corticosteroids of short time activity (metipred, hydrocortison) **leishmaniae** were revealed both in the target organs (spleen, liver, marrow) and in lungs, in cases of using the corticosteroid of prolonged activity (tricort-40) **leishmaniae** were observed also in lungs, kidneys, testis.

L40 ANSWER 3 OF 18 MEDLINE
ACCESSION NUMBER: 93032060 MEDLINE
DOCUMENT NUMBER: 93032060 PubMed ID: 1412645
TITLE: Is **leishmaniasis** ever cured?.
AUTHOR: de Rossell R A; de Duran R J; Rossell O; Rodriguez A M
CORPORATE SOURCE: Departamento de Biologia, Facultad de Ciencias, Universidad de Los Andes, La Hechicera, Merida, Venezuela.
SOURCE: TRANSACTIONS OF THE ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE, (1992 May-Jun) 86 (3) 251-3.
Journal code: 7506129. ISSN: 0035-9203.

PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199211
ENTRY DATE: Entered STN: 19930122
Last Updated on STN: 19930122
Entered Medline: 19921102

AB The persistence of parasites in mice cured of **Leishmania mexicana** infection was investigated by using **immunosuppressive** drugs and checking for the reappearance of lesions. BALB/c (susceptible) and C57BL/6 (partially resistant) mice infected with 10(4) amastigotes were treated with either thermotherapy or meglumine antimonate and subsequently **immunosuppressed** with either cyclophosphamide or **hydrocortisone**. **Immunosuppression** by either method caused lesions to reappear in both strains of mice regardless of the treatment used to produce clinical cure. In both strains of mice the proportion of animals developing lesions after **immunosuppression** was greater in the mice cured by the drug. The relevance of these findings to human therapy is discussed.

L40 ANSWER 4 OF 18 MEDLINE
ACCESSION NUMBER: 86084148 MEDLINE
DOCUMENT NUMBER: 86084148 PubMed ID: 4077160
TITLE: Role of **immunosuppression** in **Leishmania mexicana** induced lesions in hamsters.
AUTHOR: Sehgal S; Arora S K
SOURCE: INDIAN JOURNAL OF MEDICAL RESEARCH, (1985 Sep) 82 202-6.
Journal code: 0374701. ISSN: 0971-5916.
PUB. COUNTRY: India
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198602
ENTRY DATE: Entered STN: 19900321
Last Updated on STN: 19900321
Entered Medline: 19860220

L40 ANSWER 5 OF 18 MEDLINE
ACCESSION NUMBER: 71134132 MEDLINE
DOCUMENT NUMBER: 71134132 PubMed ID: 5503461
TITLE: Haematological aspects of Indian kalaazar.
AUTHOR: Chatterjea J B; Sen Gupta P C
SOURCE: JOURNAL OF THE INDIAN MEDICAL ASSOCIATION, (1970 Jun 16) 54 (12) 541-52.
Journal code: 7505608. ISSN: 0019-5847.
PUB. COUNTRY: India
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197104
ENTRY DATE: Entered STN: 19900101
Last Updated on STN: 19970203
Entered Medline: 19710425

L40 ANSWER 6 OF 18 MEDLINE
ACCESSION NUMBER: 58018631 MEDLINE
DOCUMENT NUMBER: 58018631
TITLE: Inhibition of intracutaneous **leishmanin** reaction by **hydrocortisone** acetate; comparison with cortisone, ACTH and hyaluronidase.
AUTHOR: DOSTROVSKY A; COHEN H A
SOURCE: J. Invest. Derm, (1957 July) 29 (1) 15-26.
DOCUMENT TYPE: Journal
LANGUAGE: English
FILE SEGMENT: OLDMEDLINE
OTHER SOURCE: CLML5833-18832-248-288
ENTRY MONTH: 195812
ENTRY DATE: Entered STN: 20000825
Last Updated on STN: 20000825

L40 ANSWER 7 OF 18 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2000:222028 BIOSIS
DOCUMENT NUMBER: PREV200000222028
TITLE: Effects of **immunosuppressive** therapy on murine **Leishmania infantum** visceral **leishmaniosis**.
AUTHOR(S): Gangneux, Jean-Pierre (1); Chau, Francoise; Sulahian, Annie; Derouin, Francis; Garin, Yves Jean-Francois
CORPORATE SOURCE: (1) Laboratoire de Parasitologie-Mycologie, Faculte de Medecine Lariboisiere-Saint-Louis, 15, rue de l'Ecole-de-Medecine, 75270, Paris Cedex, 06 France
SOURCE: European Cytokine Network, (Dec., 1999) Vol. 10, No. 4, pp. 557-559.
ISSN: 1148-5493.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB We evaluated the effect of **immunosuppressive** therapy on the course of infection, the spleen cell **immunophenotype** and cytokine production during murine **Leishmania infantum** visceral **leishmaniosis** (VL). Rousseau et al. (1) recently reported that prolonged administration of dexamethasone induces limited reactivation of chronic murine visceral **leishmaniosis**, with no clear Th1-Th2 cytokine patterns. We found that another glucocorticoid, **hydrocortisone** acetate, had similar effects during acute visceral **leishmaniosis**, i.e. an increase in parasite burden in the spleen, but not the liver, of infected mice. A significant increase in parasite burden in both the liver and the spleen was only achieved when mice were treated with combined dexamethasone + pentoxifylline **immunotherapy**; increases in parasite burden were never associated with a specific spleen cell **immunophenotype** or a Th1-Th2 cytokine secretion profile.

L40 ANSWER 8 OF 18 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2000:139351 BIOSIS
DOCUMENT NUMBER: PREV200000139351
TITLE: Cutaneous histoplasmosis associated with acquired **immunodeficiency** syndrome (AIDS.
AUTHOR(S): Bonifaz, Alexandro (1); Cansela, Rosalia; Novales, Josefa; Montes de Oca, Griselda; Navarrete, Gisela; Romo, Javier

CORPORATE SOURCE: (1) Zempoala 60-101, Col. Narvarte, Mexico, DF, CP 03020 Mexico
SOURCE: International Journal of Dermatology., (Jan., 2000) Vol. 39, No. 1, pp. 35-38.
ISSN: 0011-9059.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English

AB A 30-year-old man, who had originally been admitted to the Centro Dermatologico Pascua for medical attention and was later transferred to the Hospital General de Mexico, presented with a 2-month history of progressive dermatosis affecting the head (face, ear lobes, oral cavity), trunk (all faces), upper and lower limbs (including the palms and soles), external genitalia, and the perianal region. The patient had no history of homosexuality, but did have a long history of sexual intercourse with prostitutes in the city of Ciudad del Carmen (island in southeastern Mexico), where he was born and lives. The dermatosis consisted of multiple nodules and ulcerative lesions, some of them isolated and others with junctions between them, forming verrucous plaques. He complained of mild pruritus and pain. The lesions had first appeared on the face and, over the course of 2 months, had increased in size and number and were accompanied by malaise, fever, and loss of 6 kg of body weight (Fig. 1). The presumptive clinical diagnosis was **leishmaniasis**, an endemic disease in the area where he lives. Laboratory parameters at presentation included the following: hemoglobin 11.5 g/dL; hematocrit 34%; white blood cells (WBC) total 7900 cells/mm3; lymphocytes total 1414 cells/mm3; platelets 449,000/mm3; CD4+ lymphocytes 1.5% and CD8+ lymphocytes 81.0%, with a CD4/CD8 ratio of 0.18 cells/mm3. Blood chemistry, hepatic function tests, and serum electrolyte determinations were all within normal ranges. A chest roentgenogram was also normal. Human **immunodeficiency** virus (HIV) seropositivity was tested by enzyme-linked **immunosorbent** assay (ELISA) and confirmed by Western blot. Histologic evaluation showed a dense infiltration of lymphocytes and histiocytes, many of which were markedly vacuolated. A number of intracellular yeast-like cells that were easily stained with hematoxylin and eosin and periodic acid-Schiff (PAS) were evident inside the histiocytes (Fig. 2). We concluded that the granulomatous process was suggestive of histoplasmosis. Histoplasma capsulatum was eventually cultured from the skin biopsy specimens. A histoplasmin skin test was negative; precipitin and complement fixation tests using the same antigen were both positive, the latter with an initial titer of 1 : 320. The confirmatory diagnosis of acquired **immunodeficiency** syndrome (AIDS)-associated cutaneous histoplasmosis prompted us to begin treatment with amphotericin B 1 mg/kg/day, heparin 5 IU/day, **hydrocortisone** 500 mg/day, and itraconazole 400 mg/day. Also, the main laboratory tests were repeated. When an accumulated dose of 535 mg of amphotericin B had been reached, an elevation of serum creatinine to 1.48 mg/dL occurred, and a glomerular filtration rate of 57.8%, a urinary volume of 1350 mL/24 h, and a potassium (K) of 2.3 mEq/L were found. For this reason, the amphotericin B dose was reduced to 0.50 mg/kg/day, and potassium replacement was started. The reduced amphotericin B dose resulted in an improvement in the serum creatinine to 0.9 mg/dL, a glomerular filtration rate of 92.5%, a urinary volume of 2900 mL/24 h, and a potassium level of 4.3 mEq/L. Despite the abnormalities detected in the laboratory tests, the

patient showed a clear clinical improvement and his complement fixation ratio to histoplasmin decreased from 1 : 320 to 1 : 64. Currently, the patient is being maintained with a 300-mg/day dose of itraconazole, and is being periodically re-evaluated by laboratory testing. He shows good clinical progress and resolution of most lesions (Fig. 3).

L40 ANSWER 9 OF 18 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1986:145037 BIOSIS
DOCUMENT NUMBER: BA81:55453
TITLE: ROLE OF **IMMUNOSUPRESSION** IN **LEISHMANIA-MEXICANA** INDUCED LESIONS IN HAMSTERS.
AUTHOR(S): SEHGAL S; ARORA S K
CORPORATE SOURCE: POSTGRADUATE INST. MED. EDUCATION RES., CHANDIGARH 160012.
SOURCE: INDIAN J MED RES, (1985) 82 (SEPT), 202-206.
CODEN: IJMRAQ. ISSN: 0019-5340.
FILE SEGMENT: BA; OLD
LANGUAGE: English
AB The foot-pad lesions in hamsters infected with **L. mexicana** amazonensis were facilitated by **immunosuppression** using **hydrocortisone**. However, the appearance of lesions of **L. mexicana** was not uniformly predictable in tropical climates. The animals with skin lesions had abundant circulating anti-**leishmanial antibodies** which had no direct correlation with the parasite burden. The kidneys of these animals did not reveal significant **immune** complex deposition. There was a very close antigenic similarity between **L. donovani** and **L. mexicana**.

L40 ANSWER 10 OF 18 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2002064208 EMBASE
TITLE: A case of visceral **leishmaniasis** with protracted incubation in a nonendemic area.
AUTHOR: Cainelli F.; Concia E.; Vento S.
CORPORATE SOURCE: F. Cainelli, Section of Infectious Diseases, Department of Pathology, University of Verona, Via Vasco de Gama 7, 37138 Verona, Italy. francescacainelli@yahoo.it
SOURCE: European Journal of Clinical Microbiology and Infectious Diseases, (2001) 20/12 (908-909).
Refs: 6
ISSN: 0934-9723 CODEN: EJCDEU
COUNTRY: Germany
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
006 Internal Medicine
037 Drug Literature Index
LANGUAGE: English

L40 ANSWER 11 OF 18 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2001304553 EMBASE
TITLE: New advances in systemic antifungal therapy.
AUTHOR: Kung H.-C.; Chen Y.-C.
CORPORATE SOURCE: H.-C. Kung, Department of Internal Medicine, National Taiwan University Hospital, Taipei, Taiwan,Province

of China
SOURCE: Journal of Internal Medicine of Taiwan, (2001) 12/3 (132-141).
Refs: 18
ISSN: 1016-7390 CODEN: JIMTB3
COUNTRY: Taiwan,Province of China
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
026 Immunology, Serology and Transplantation
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
039 Pharmacy
LANGUAGE: English
SUMMARY LANGUAGE: English
AB With the growing proportion of **immunocompromised** patients due to cytotoxic chemotherapy, organ transplantation, and AIDS, the number of invasive diseases due to various kinds of fungi has increased gradually during the past years, especially aspergillosis and candidiasis. There are mainly two categories of drugs in systemic antifungal therapy: polyenes, which included amphotericin B deoxycholate and new lipid formulations of amphotericin B; and azoles, which include fluconazole and itraconazole. Intravenous amphotericin B deoxycholate has been the standard therapy for most serious fungal infections since the 1950s. However, many adverse effects, especially nephrotoxicity and infusion-related events, frequently limit its use. Recently, less nephrotoxic lipid formulations have been introduced. They can allow safer delivery of effective doses and exploring escalating doses for less susceptible pathogens or refractory infections. The azole antifungal drugs have revolutionized the therapy of fungal diseases, especially fluconazole and itraconazole. They are well tolerated, orally administered, and have a broad spectrum. These new antifungal agents offer alternative therapy to amphotericin B for many invasive fungal diseases, and in some instances have become the preferred agents for the treatment of less severe, disseminated fungal infection.

L40 ANSWER 12 OF 18 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 95280865 EMBASE
DOCUMENT NUMBER: 1995280865
TITLE: Efficacy of permethrin-impregnated uniforms in the prevention of malaria and **leishmaniasis** in Colombian soldiers.
AUTHOR: Soto J.; Medina F.; Dember N.; Berman J.
CORPORATE SOURCE: Apartado Aereo 58537,Bogota, Colombia
SOURCE: Clinical Infectious Diseases, (1995) 21/3 (599-602).
ISSN: 1058-4838 CODEN: CIDIEL
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
017 Public Health, Social Medicine and Epidemiology
035 Occupational Health and Industrial Medicine
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB We determined the efficacy of the use of permethrin-impregnated uniforms for prevention of malaria and **leishmaniasis** in a

double-blind, randomized study of Colombian soldiers on patrol. In the study of malaria, soldiers were issued impregnated uniforms (i.e., a shirt, an undershirt, pants, socks, and a hat) or uniforms washed in water; the soldiers wore the uniforms day and night for a mean of 4.2 weeks and were observed for an additional 4 weeks. Three (3%) of 86 soldiers wearing impregnated uniforms contracted malaria, whereas 12 (14%) of 86 soldiers wearing control uniforms contracted malaria (P = .015). In the study of **leishmaniasis** (soldiers were in the area of endemicity for 6.6 weeks and were observed for 12 weeks thereafter), 4 (3%) of 143 soldiers wearing impregnated uniforms and 18 (12%) of 143 soldiers wearing control uniforms acquired disease (P = .002). In the **leishmaniasis** study, and presumably in the malaria study, breakthrough infections in the treated group were primarily due to bites in unclothed regions of the body (face and hands). Permethrin-treated uniforms were virtually nontoxic (there were only two cases of mild skin irritation among 229 subjects), and impregnation is quick and inexpensive. Impregnation of clothing with permethrin is suggested for nonimmune populations who are likely to be exposed to malaria or **leishmaniasis** over a period of 1-2 months.

L40 ANSWER 13 OF 18 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 95112337 EMBASE
DOCUMENT NUMBER: 1995112337
TITLE: **Immunochemotherapy** for a systemic intracellular infection: Accelerated response using interferon-.gamma. in visceral **leishmaniasis**
.
AUTHOR: Sundar S.; Rosenkaimer F.; Lesser M.L.; Murray H.W.
CORPORATE SOURCE: Cornell University Medical College, 1300 York Ave.,New York, NY 10021, United States
SOURCE: Journal of Infectious Diseases, (1995) 171/4 (992-996).
ISSN: 0022-1899 CODEN: JIDIAQ
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English

AB To determine if cytokine **immunotherapy** accelerates the response to conventional treatment in visceral **leishmaniasis** (kala-azar), previously untreated Indian patients were given antimony for 30 days (n = 15)or antimony plus interferon-.gamma.(IFN-.gamma.; n = 16). After 10 days, 10(63%) of 16 patients treated with antimony plus IFN-.gamma. versus 1 (7%) of 15 randomized to antimony alone were considered cured of parasites (P < .005). On day 20, 14 (93%) of 15 versus 6 (40%) of 15 patients, respectively, were apparent clinical cures (P < .006), and treatment was discontinued early in the 14 IFN-.gamma.-treated responders. Day 30 apparent cure rates (100% vs. 73%) and 6-month ultimate cure responses (87% vs. 60%) were higher in IFN-.gamma.-treated patients but not statistically different from controls (P > .05). All 13 IFN-.gamma.-treated subjects who were cured (12 of whom received therapy for 20 days) have remained healthy with follow-up of 14-24 months (mean, 18.9). These results indicate that IFN-.gamma. successfully accelerates the parasitologic and clinical response to

antimony treatment, an effect that should permit shortening the duration of conventional therapy in previously untreated kala-azar.

L40 ANSWER 14 OF 18 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 93177939 EMBASE
DOCUMENT NUMBER: 1993177939
TITLE: Antimicrobial and **immunopathologic** effects of cytokine-induced nitric oxide synthesis.
AUTHOR: Green S.J.; Nacy C.A.
CORPORATE SOURCE: EntreMed Inc, 9610 Medical Center Drive,Rockville, MD 20850, United States
SOURCE: Current Opinion in Infectious Diseases, (1993) 6/3 (384-396).
ISSN: 0951-7375 CODEN: COIDE5
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 004 Microbiology
026 Immunology, Serology and Transplantation
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Despite its small size and transitory nature, nitric oxide is an enormously versatile effector molecule: it acts as a sensory transmitter, provokes vasodilation, influences clotting and cell adhesion, serves as a host-defense molecule, and contributes to **immunosuppression** and neurotoxicity. In the past decade, researchers have identified the cell sources, dissected the biochemical pathways, and characterized a number of physiologic, pharmacologic, and pathologic effects of nitric oxide. This past year was highlighted by reports on the molecular cloning and functional expression of various nitric oxide synthase isoforms. With the recent publication of comprehensive reviews, we selected current papers documenting both the cytotoxic effects of cytokine-induced nitric oxide synthesis and the mechanisms that control this event during an **immune** response.

L40 ANSWER 15 OF 18 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 2003-210356 [20] WPIDS
DOC. NO. CPI: C2003-053734
TITLE: New infectable human hepatoma cell line, useful e.g. as model for drug screening, for diagnosis and testing, production of **vaccines** and in extracorporeal bioreactors.
DERWENT CLASS: B04 D16 D22 J04
INVENTOR(S): GRIPON, P; GUGUEN-GUILLOUZO, C; RUMIN, S; TREPO, C
PATENT ASSIGNEE(S): (INRM) INSERM INST NAT SANTE & RECH MEDICALE
COUNTRY COUNT: 26
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2003004627	A2	20030116	(200320)*	FR	74

RW: AT BE BG CH CY CZ DE DK EE ES FI FR GB GR IE IT LU MC NL PT SE SK TR
W: CA JP US

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003004627 A2		WO 2002-FR2391	20020708

PRIORITY APPLN. INFO: FR 2001-9044 20010706
AN 2003-210356 [20] WPIDS
AB WO2003004627 A UPAB: 20030324
NOVELTY - Human hepatoma cell lines (A) that can be infected naturally with (i) parasites, hepatotropic or not, e.g. Plasmodium or **Leishmania** or (ii) viruses. They express receptors for Flaviviridae and Hepadnaviridae, particularly hepatitis B and C viruses.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) human hepatoma cell lines (B) that:

(i) can differentiate to cells having morphology similar to that of liver cells (hepatocytes and/or biliary cells);

(ii) express functions characteristic of hepatocytes; or

(iii) in the proliferative stage, have the properties of pluripotent cells;

(2) cells and their components derived from (A) or (B);

(3) selecting (A) or (B);

(4) infecting hepatic cells with a hepatotropic parasite or virus;

(5) transforming (A), (B) or the cells of (2) with a vector containing at least part of the genetic material of hepatitis B or C virus (HBV, HCV);

(6) use of specific medium (X) for maintaining stability of (A), (B) or the cells of (2);

(7) **antibodies** (Ab) directed against Flaviviridae or Hepadnaviridae obtained from (A), (B) or the cells of (2);

(8) viral neutralization test;

(9) **vaccine** containing viral particles and/or polypeptides obtained by infection or transfection of (A), (B) and/or cells of (2); and

(10) evaluating virucidal activity of chemical disinfectants.

ACTIVITY - Virucide; Hepatotropic; Antiinflammatory. No relevant biological data is given.

MECHANISM OF ACTION - **Vaccine**.

USE - (A) are used:

(i) to prepare chips for high-throughput screening of differentially expressed genes;

(ii) to perform metabolic/toxicity tests, for evaluating new pharmaceuticals, food components and/or environmental pollutants;

(iii) to produce extracorporeal bioreactors for treating acute liver failure;

(iv) to screen for/produce new **vaccines** and antiviral agents; and

(v) to test efficacy of chemical antiviral disinfectants.

Antibodies (Ab) raised against virus produced in (A) are used in a viral neutralization tests and viral particles/polypeptides generated in (A) are used to make **vaccines**. (All claimed).

ADVANTAGE - (A) and related cell lines grow well; can be infected with viruses or pathogens and have all the biochemical properties of hepatic cells, so are nearly ideal models for such

cells.
Dwg.0/18

L40 ANSWER 16 OF 18 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 2002-599627 [64] WPIDS
DOC. NO. CPI: C2002-169448
TITLE: Film forming treatment composition, useful for treating nail or skin disorders, e.g. psoriasis, skin cancers, warts or eczema, comprises film former, plasticizer, urea, solvent/volatile carrier and therapeutic substance.
DERWENT CLASS: A96 B07
INVENTOR(S): DVORETZKY, I; KULEZA, J E
PATENT ASSIGNEE(S): (DVOR-I) DVORETZKY I; (KULE-I) KULEZA J E
COUNTRY COUNT: 92
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002055023	A2	20020718	(200264)*	EN	26

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002055023	A2	WO 2002-US282	20020107

PRIORITY APPLN. INFO: US 2001-260430P 20010109
AN 2002-599627 [64] WPIDS
AB WO 200255023 A UPAB: 20021007
NOVELTY - A film forming treatment composition (I), comprises (w/v.%):
(A) a film former (0.5 - 25);
(B) a plasticizer (0.5 - 25);
(C) urea (0.5 - 20);
(D) a solvent/volatile carrier (40 - 90); and
(E) at least one therapeutic substance.
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a treatment system (II), comprising:
(a) (I);
(b) a heat generating pad (A), which incorporates a heat producing device and is constructed for delivering the desired level of heat upon activation; and
(c) a holding and supporting member (B) constructed for:
(i) cooperating with (A) for enabling the application of heat directly to a desired application site of the film forming composition; and
(ii) being securely retained on a portion of the human body in overlying engagement with the heat delivery patch/pad and the film forming composition.
ACTIVITY - Dermatological; Antipsoriatic; Cytostatic; Virucide;

Antibacterial; Protozoacide; Antiinflammatory.

No biological data available.

MECHANISM OF ACTION - None given.

USE - (I) is used for providing transdermal delivery of a desired therapeutic agent (claimed) to humans for treating wide variety of medical conditions including psoriasis, skin cancers, warts, **leishmaniasis**, mycobacteria and granuloma annulare, Lichen Planus or eczema with nail involvement.

ADVANTAGE - (I) provides a safe, effective and cost efficient treatment system for nails and nail diseases.

Dwg.0/0

L40 ANSWER 17 OF 18 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 2001-536498 [59] WPIDS
DOC. NO. CPI: C2001-159724
TITLE: Drug and heat therapy treatment system comprising an exothermic pad, useful for treating e.g. psoriasis, skin cancers, warts.
DERWENT CLASS: A96 B05
INVENTOR(S): DVORETZKY, I; KULEZA, J E
PATENT ASSIGNEE(S): (DVOR-I) DVORETZKY I; (KULE-I) KULEZA J E
COUNTRY COUNT: 92
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001058408	A2	20010816	(200159)*	EN	35
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW					
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW					
AU 2001036627	A	20010820	(200175)		
US 2001049546	A1	20011206	(200203)		
EP 1255519	A2	20021113	(200282)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR					

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 2001058408	A2		WO 2001-US3432	20010202
AU 2001036627	A		AU 2001-36627	20010202
US 2001049546	A1	Provisional	US 2000-181048P	20000208
			US 2001-756059	20010108
EP 1255519	A2		EP 2001-908795	20010202
			WO 2001-US3432	20010202

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2001036627	A	Based on	WO 200158408
EP 1255519	A2	Based on	WO 200158408

PRIORITY APPLN. INFO: US 2001-756059 20010108; US 2000-181048P

20000208

AN 2001-536498 [59] WPIDS

AB WO 200158408 A UPAB: 20011012

NOVELTY - A heat therapy system comprising an exothermic pad or heat delivery patch provides controlled heat delivery for direct treatment of medical conditions, and improves or enhances the penetration of systemic and topical medications.

DETAILED DESCRIPTION - A treatment system for providing heat therapy for a variety of medical conditions comprises a member for holding and supporting a heat delivering patch or exothermic pad, enabling application of heat directly to a precisely desired location, a means for securing the patch/pad and optionally a systemic or topical medication.

ACTIVITY - Antipsoriatic; cytotoxic; dermatological; virucide.

MECHANISM OF ACTION - None given in the source material.

USE - For treating a variety of medical conditions which can be treated or improved by heat penetration into the skin, subcutaneous tissues, joints, muscles or blood stream, e.g. psoriasis, skin cancers, warts, **leishmaniasis**, mycobacteria and granuloma annulare.

Dwg.0/5

L40 ANSWER 18 OF 18 WPIDS (C) 2003 THOMSON DERWENT

ACCESSION NUMBER: 1998-261191 [23] WPIDS

CROSS REFERENCE: 1996-497242 [49]

DOC. NO. CPI: C1998-081104

TITLE: **Vaccine** compositions containing soluble aluminium salt - used for treating humans and animals suffering from, e.g. rabies, influenzae or Aujesky's disease.

DERWENT CLASS: A96 B04 B05 C03 C06 D16

INVENTOR(S): AUCOUTURIER, J; GANNE, V

PATENT ASSIGNEE(S): (SEPP) SEPPIC SOC EXPL PROD IND CHIM

COUNTRY COUNT: 20

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9817311	A1	19980430	(199823)*	FR	25
RW: AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE					
W: BR JP					
FR 2754715	A1	19980424	(199823)		
EP 939649	A1	19990908	(199941)	FR	
R: BE DE ES FR GB IT NL					
BR 9712546	A	19991019	(200008)		
JP 2000507610	W	20000620	(200036)		20
US 6117432	A	20000912	(200046)		
EP 939649	B1	20020403	(200230)	FR	
R: BE DE ES FR GB IT NL					
DE 69711673	E	20020508	(200238)		
JP 3329471	B2	20020930	(200271)		8

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9817311	A1	WO 1997-FR1816	19971010
FR 2754715	A1	FR 1996-12718	19961018

Searcher : Shears 308-4994

EP 939649	A1		EP 1997-909390	19971010
			WO 1997-FR1816	19971010
BR 9712546	A		BR 1997-12546	19971010
			WO 1997-FR1816	19971010
JP 2000507610	W		WO 1997-FR1816	19971010
			JP 1998-519016	19971010
US 6117432	A	CIP of	US 1995-478091	19950607
			US 1997-795931	19970205
EP 939649	B1		EP 1997-909390	19971010
			WO 1997-FR1816	19971010
DE 69711673	E		DE 1997-611673	19971010
			EP 1997-909390	19971010
			WO 1997-FR1816	19971010
JP 3329471	B2		WO 1997-FR1816	19971010
			JP 1998-519016	19971010

FILING DETAILS:

PATENT NO	KIND		PATENT NO
EP 939649	A1	Based on	WO 9817311
BR 9712546	A	Based on	WO 9817311
JP 2000507610	W	Based on	WO 9817311
EP 939649	B1	Based on	WO 9817311
DE 69711673	E	Based on	EP 939649
		Based on	WO 9817311
JP 3329471	B2	Previous Publ.	JP 200007610
		Based on	WO 9817311

PRIORITY APPLN. INFO: FR 1996-12718 19961018; FR 1995-4739 19950420

AN 1998-261191 [23] WPIDS

CR 1996-497242 [49]

AB WO 9817311 A UPAB: 20021105

New compositions comprising: (i) at least one antigen or in vivo generator of an amino acid sequence, and (ii) an adjuvant which is a water-soluble trivalent metal salt with a pharmaceutically acceptable organic anion. Also claimed are compositions similar to above, but further comprising a sympathomimetic amine selected from catecholamine, amphetamine, phenyl isopropylamine, tyramine, especially ephedrine, isoproterenol, L-**Epinephrine**, levarterenol, phenylephedrine and salbutamol.

USE - The compositions may be used for treatment of humans and animals suffering from: (i) viral infections such as rabies, herpes, influenzae, foot and mouth disease, Aujesky's disease, and HIV; (ii) bacterial infections caused by Escherichia coli, Pasteurella, Furonculosis, Vibriosis, Staphylococcus and Streptococcus, and (iii) parasitic disorders caused by Trypanosoma, Plasmodium, **Leishmania** and salmon lice.

ADVANTAGE - The compositions are capable of increasing the **immune** response without risk the risk of development of local lesions or other reactions, and inducing cellular as well as humoral **immunity**.

Dwg.0/0

(FILE 'MEDLINE' ENTERED AT 11:57:35 ON 08 MAY 2003)

L41 3394 SEA FILE=MEDLINE ABB=ON PLU=ON LEISHMANIA/CT

L42 3186 SEA FILE=MEDLINE ABB=ON PLU=ON LEISHMANIASIS/CT

L43	39210	SEA FILE=MEDLINE ABB=ON	PLU=ON	EPINEPHRINE/CT	
L44	2359	SEA FILE=MEDLINE ABB=ON	PLU=ON	DIPHENHYDRAMINE/CT	
L45	17935	SEA FILE=MEDLINE ABB=ON	PLU=ON	PREDNISOLONE/CT	
L46	42494	SEA FILE=MEDLINE ABB=ON	PLU=ON	HYDROCORTISONE/CT	
L47	7959	SEA FILE=MEDLINE ABB=ON	PLU=ON	ACETAMINOPHEN/CT	
L48	3	SEA FILE=MEDLINE ABB=ON	PLU=ON	(L41 OR L42) AND (L43 OR L44 OR L45 OR L46 OR L47)	

L41	3394	SEA FILE=MEDLINE ABB=ON	PLU=ON	LEISHMANIA/CT	
L42	3186	SEA FILE=MEDLINE ABB=ON	PLU=ON	LEISHMANIASIS/CT	
L49	48392	SEA FILE=MEDLINE ABB=ON	PLU=ON	ANTIGENS/CT	
L50	161	SEA FILE=MEDLINE ABB=ON	PLU=ON	(L41 OR L42) AND L49	
L51	105400	SEA FILE=MEDLINE ABB=ON	PLU=ON	SKIN/CT	
L52	1	SEA FILE=MEDLINE ABB=ON	PLU=ON	L50 AND L51	

L53 4 L48 OR L52

L53 ANSWER 1 OF 4 MEDLINE
AN 89055544 MEDLINE
TI Behavior of Leishmania braziliensis s.l. in golden hamsters: evolution of the infection under different experimental conditions.
AU Travi B; Rey-Ladino J; Saravia N G
SO JOURNAL OF PARASITOLOGY, (1988 Dec) 74 (6) 1059-62.
Journal code: 7803124. ISSN: 0022-3395.
AB Reproducibility of Leishmania braziliensis s.l. metastatic behavior in hamsters was studied for 9 isolates of L.b. panamensis and 2 of L.b. guyanensis with a previous record of metastasis. Also, the influence of corticosteroids and trauma was evaluated. In the corticosteroid-treated group, metastases appeared earlier than in the nontreated group, and localization at the site of trauma was more frequent (4/9) than in the nontreated hamsters (1/5). Nine of the 11 strains (82%) were capable of reproducing metastatic behavior. Studies on dissemination of L. b. panamensis showed that the regional lymph node is invaded as soon as 5 days postinfection, with further nonhematic dissemination to other tissues and organs in less than 4 wk.

L53 ANSWER 2 OF 4 MEDLINE
AN 86084148 MEDLINE
TI Role of immunosuppression in Leishmania mexicana induced lesions in hamsters.
AU Sehgal S; Arora S K
SO INDIAN JOURNAL OF MEDICAL RESEARCH, (1985 Sep) 82 202-6.
Journal code: 0374701. ISSN: 0971-5916.

L53 ANSWER 3 OF 4 MEDLINE
AN 84257423 MEDLINE
TI Cutaneous leishmaniasis: immune complex formation and necrosis in the acute phase.
AU Ridley M J; Ridley D S
SO BRITISH JOURNAL OF EXPERIMENTAL PATHOLOGY, (1984 Jun) 65 (3) 327-36.
Journal code: 0372543. ISSN: 0007-1021.
AB Twenty biopsies of lesions of cutaneous leishmaniasis were classified according to the mechanism of parasite elimination, on the basis of macrophage activation (five cases) or macrophage lysis (15 cases). The immunoperoxidase technique was used to demonstrate free Leishmania antigen, immunoglobulins, complement, lysozyme,

C-reactive protein, beta-lipoprotein, alpha 1-antitrypsin, alpha 2-macroglobulin, plasminogen and factor VIII, which were quantitated and comparatively assessed. The fall in the parasite load during the course of the infection was associated with rising levels of IgG, IgM and IgE, and of the complement components of the classical pathway. Macrophage lysis supervened when there was an approximate equivalence of antigen and antibody, and was associated with the deposition of immune complex components. Lysis of the acute focal type (C response) was accompanied by a massive liberation of free Leishmania antigen, followed by a fall indicative of parasite elimination. The lysis of small numbers of macrophages scattered diffusely in the lesion, which was slow to reach completion (B response), was less effective and immunologically closer to the non-lytic (A) response. A terminal fall of the immunological factors other than the globulins, suggestive of resolution, was observed mainly in the C response. Lymphocytes may be important in macrophage activation associated with the macrophage A response and in the later stage of the B and C responses. However immunologically induced host-cell lysis is more important than macrophage activation for the elimination of Leishmania in the acute stage of most skin lesions. It is associated with, and may be caused by, the formation in situ of immune complexes of Leishmania antigen and antibody at an appropriate ratio.

L53 ANSWER 4 OF 4 MEDLINE
AN 68313740 MEDLINE
TI The treatment of late cutaneous leishmaniasis by simultaneous intralesional steroid and intramuscular antimony.
AU Dostrovsky A; Cohen H A
SO DERMATOLOGIA INTERNATIONALIS, (1967 Jul-Sep) 6 (3) 172-3.
Journal code: 0243670. ISSN: 0096-1108.

(FILE 'HCAPLUS, MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO' ENTERED AT 12:03:44 ON 08 MAY 2003)

L54 305 S "MAGILL A"?/AU
L55 56 S "STITELER J"?/AU
L56 268 S "GROGL M"?/AU
L57 298 S "ECKELS K"?/AU
L58 471 S "BALLOU W"?/AU
L59 1 S L54 AND L55 AND L56 AND L57 AND L58
L60 47 S L54 AND (L55 OR L56 OR L57 OR L58)
L61 4 S L55 AND (L56 OR L57 OR L58)
L62 2 S L56 AND (L57 OR L58)
L63 1 S L57 AND L58
L64 291 S (L60 OR L54 OR L55 OR L56 OR L57 OR L58) AND L22
L65 7 S L64 AND (LYSATE OR SLURR? OR L32)
L66 9 S L59 OR L61 OR L62 OR L63 OR L65
L67 5 DUP REM L66 (4 DUPLICATES REMOVED)

Author(s)

L67 ANSWER 1 OF 5 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2003:300426 HCAPLUS
TITLE: Microfluidized **Leishmania lysate** prepn. methods and uses thereof
INVENTOR(S): **Magill, Alan J.; Stiteler, John M.; Grogl, Max;** Rowton, Edgar D.; **Eckels, Kenneth H.; Ballou, William R.**
PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 11 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003072714	A1	20030417	US 2001-975020	20011012
WO 2003033533	A1	20030424	WO 2001-US31894	20011012

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-975020 A 20011012

AB Disclosed is the method for prepn. of microfluidized **Leishmania** parasite **lysate**, in particular as it relates to use of the prepns. for assays and immunogenic compns. Also disclosed are methods of using the microfluidized **lysate** prepns. in skin test antigen assays as well as kits comprising the microfluidized **lysate** prepns. The specific examples include the process for making **L. guyanensis** microfluidized **lysate**; prodn. of heat-treated **L. mexicana** skin test injectable; skin test antigen assay in small group of human subjects; and heat-treated **Leishmania** skin test injectable study in a larger group of patients including disease active subjects, healthy **leishmania** subjects, and healed **leishmania** subjects. The microfluidized **lysate** prepns. are made under current good manufg. practice and may therefore be standardized and such prepns. may be produced with consistency.

L67 ANSWER 2 OF 5 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:14414 BIOSIS
DOCUMENT NUMBER: PREV200100014414
TITLE: ODS **Leishmania** skin test, MFL-LSTA(R2): Stability of the cGMP product in the guinea pig animal model.
AUTHOR(S): **Stiteler, J. M. (1); Grogl, M.;** Rowton, E. D.
CORPORATE SOURCE: (1) Department of Entomology, Division of Communicable Diseases and Immunology, Walter Reed Army Institute of Research, Washington, DC USA
SOURCE: American Journal of Tropical Medicine and Hygiene, (March, 2000) Vol. 62, No. 3 Supplement, pp. 310. print.
Meeting Info.: 49th Annual Meeting of the American Society of Tropical Medicine and Hygiene Houston, Texas, USA October 29-November 02, 2000 American Society of Tropical Medicine and Hygiene

. ISSN: 0002-9637.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L67 ANSWER 3 OF 5 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1999:503816 BIOSIS
DOCUMENT NUMBER: PREV199900503816
TITLE: Current Good Manufacturing Practices (cGMP) production of a heat-treated Leishmania skin test, MFL-LSTA(R2.
AUTHOR(S): **Stiteler, J. M. (1)**; Rowton, E. D.; **Grogl, M.**; **Eckels, K. H.**; Martin, S. K.; Miller, R.; Magill, A. J.
CORPORATE SOURCE: (1) Department of Entomology, Walter Reed Army Institute of Research, Washington, DC USA
SOURCE: American Journal of Tropical Medicine and Hygiene, (Sept., 1999) Vol. 61, No. 3 SUPPL., pp. 456-457. Meeting Info.: 48th Annual Meeting of the American Society of Tropical Medicine and Hygiene Washington, D.C., USA November 28-December 2, 1999 American Society of Tropical Medicine and Hygiene
. ISSN: 0002-9637.
DOCUMENT TYPE: Conference
LANGUAGE: English

L67 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2003 ACS DUPLICATE 1
ACCESSION NUMBER: 1995:757480 HCAPLUS
DOCUMENT NUMBER: 123:336863
TITLE: Characterization of a **Leishmania tropica** antigen that detects immune responses in Desert Storm viscerotropic **leishmaniasis** patients
AUTHOR(S): Dillon, Davin C.; Day, Craig H.; Whittle, Jacqueline A.; **Magill, Alan J.**; Reed, Steven G.
CORPORATE SOURCE: Infectious Disease Research Inst., Seattle, WA, 98104, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1995), 92(17), 7981-5
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A chronic debilitating parasitic infection, viscerotropic **leishmaniasis** (VTL), has been described in Operation Desert Storm veterans. Diagnosis of this disease, caused by **Leishmania tropica**, has been difficult due to low or absent specific immune responses in traditional assays. The authors report the cloning and characterization of two genomic fragments encoding portions of a single 210-kDa **L. tropica** protein useful for the diagnosis of VTL in U.S. military personnel. The recombinant proteins encoded by these fragments, recombinant (r) Lt-1 and rLt-2, contain a 330-amino acid repeat that reacts with sera from Desert Storm VTL patients and with sera from **L. tropica**-infected patients with cutaneous **leishmaniasis**. Antibody reactivities to rLt-1

indicated a bias toward IgG2 in VTL patient sera. Peripheral blood mononuclear cells from VTL patients produced interferon .gamma., but not interleukin 4 or 10, in response to rLt-1. No cytokine prodn. was obsd. in response to parasite **lysate**. The results indicate that specific **leishmanial** antigens may be used to detect immune responses in VTL patients with chronic infections.

L67 ANSWER 5 OF 5	CONFSCI COPYRIGHT 2003 CSA
ACCESSION NUMBER:	2000:70783 CONFSCI
DOCUMENT NUMBER:	00-067654
TITLE:	Ods Leishmania skin test, MFL-LSTA[R2]: Stability of the cGMP product in the guinea pig animal model
AUTHOR:	**Stiteler, J.M.; Grogl, M.;** Rowton, E.D.
CORPORATE SOURCE:	Dep. Entomology, Division Communicable Diseases & Immunology, Walter Reed Army Inst. Res. Washington, DC, USA
SOURCE:	American Society of Tropical Medicine and Hygiene, 3088 Briarcliff Rd., Ste. 11A, Atlanta, GA 30329, USA Meeting Info.: 000 5172: ASTMH 49th Annual Meeting (0005172). Houston, Texas (USA). 29 Oct-2 Nov 2000. American Society of Tropical Medicine and Hygiene.
DOCUMENT TYPE:	Conference
FILE SEGMENT:	DCCP
LANGUAGE:	English

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